

PERCUTANEOUS ULTRASOUND-GUIDED RADIOFREQUENCY ABLATION OF INTRAHEPATIC CHOLANGIOCARCINOMA

Yi-You Chiou,^{1,3} Jen-I Hwang,^{2,3} Yi-Hong Chou,^{1,3} Hsin-Kai Wang,^{1,3} Jen-Huey Chiang,^{1,3}
and Cheng-Yen Chang^{1,3}

¹Department of Radiology, Taipei Veterans General Hospital, Taipei,

²Department of Radiology, Taichung Veterans General Hospital, Taichung, and

³National Yang-Ming University School of Medicine, Taipei, Taiwan.

This study evaluated the clinical applications, treatment effects, and complications of percutaneous ultrasound (US)-guided radiofrequency ablation (RFA) of intrahepatic cholangiocarcinoma. Ten patients (6 men and 4 women) with histologically proven cholangiocarcinoma underwent US-guided percutaneous RFA. Tumor diameters ranged from 1.9 to 6.8 cm. There were 12 sessions of RFA for 10 solitary cholangiocarcinomas. Eight patients were treated at a single session and two patients had two treatment sessions. The efficacy of RFA was evaluated using contrast-enhanced dynamic computed tomography 1 month after treatment and then every 3 months. Complete necrosis was defined as lack of contrast enhancement of the treated region. There was complete necrosis in eight tumors. In two patients with large tumors (4.7 and 6.8 cm in diameter), enhancement of residual tissue was observed after RFA treatment, indicating residual tumor. Complete necrosis was seen in all five tumors (100%) with diameters of 3.0 cm or less, two of three tumors (67%) with diameters of 3.1–5.0 cm, and one of two tumors (50%) with diameters of more than 5.0 cm. A large biloma was found in one patient after treatment. No serious complications occurred in the other nine patients. In conclusion, percutaneous RFA is effective and successful in the treatment of intrahepatic cholangiocarcinoma of 3 cm or less and satisfactory for tumors of 3–5 cm. The rate of serious complications after RFA is low. Further follow-up is necessary to determine long-term efficacy.

Key Words: cholangiocarcinoma, liver, neoplasm, radiofrequency ablation
(*Kaohsiung J Med Sci* 2005;21:304–9)

Cholangiocarcinoma is the second most common primary hepatic neoplasm [1]. Surgical resection of the tumor offers the best chance for long-term survival. However, patients with liver cirrhosis or chronic hepatitis are not candidates for surgical resection because of poor hepatic reserve [2,3]. The alternative technique, radiofrequency ablation (RFA), is a relatively new, minimally invasive therapy for primary

and metastatic liver tumors. Percutaneous RFA for hepatic neoplasm is a recent innovation, but the results of preliminary clinical series and animal studies are encouraging and show that it is technically feasible and has minimal morbidity [4–8].

Although RFA is effective in the treatment of hepatocellular carcinoma and liver metastasis, to the best of our knowledge, its clinical efficacy in the treatment of intrahepatic cholangiocarcinoma has not been reported. The purpose of this paper is to describe our experience with percutaneous ultrasound (US)-guided RFA in intrahepatic cholangiocarcinoma and to report on the technique, its complications, and efficacy.

Received: March 3, 2005

Accepted: May 13, 2005

Address correspondence and reprint requests to: Dr. Yi-Hong Chou, Department of Radiology, Taipei Veterans General Hospital, 201 Shih-Pai Road, Section 2, Taipei 112, Taiwan.

E-mail: yychiou@vghtpe.gov.tw

MATERIALS AND METHODS

Patients

From January 2002 to October 2004, 10 patients underwent percutaneous US-guided RFA to treat intrahepatic cholangiocarcinoma. The study was approved by our institutional review board, and informed consent was obtained from all patients before the procedure. Of the 10 patients, two patients refused surgery and the other eight were not considered surgical candidates because of advanced age and either comorbid conditions (4 patients) or poor hepatic reserve (4 patients). No tumors were located near the intrahepatic great vessels.

There were six men and four women with a mean age of 66.2 years (range, 38–86 years) (Table). All 10 patients had pathologic confirmation of the diagnosis from US-guided biopsy performed, either in advance or at the time of RFA. Tumor size ranged from 1.9 to 6.8 cm (mean, 3.4 cm). Tumors were classified into three groups depending on size: five tumors had a diameter of 3 cm or less, three tumors were between 3.1 and 5 cm, and two tumors were larger than 5 cm.

Radiofrequency tumor ablation technique

All patients were interviewed before treatment by one of the two experienced interventional radiologists (Yi-You Chiou, YYC; and Yi-Hong Chou, YHC), and were assessed with US before the procedure to determine whether the tumor was amenable to ablation under US guidance. Nine patients received meperidine analgesia and one patient was under conscious sedation (with droperidol, midazolam and fentanyl), administered and monitored by

anesthesiologists.

Two different RFA devices were used with techniques that have been described previously [9,10]: the RITA (radiofrequency interstitial tissue ablation) device (Rita Medical Systems, Mountain View, CA, USA) and the Radionics device (Radionics, Burlington, MA, USA). With the RITA device, ablation was performed using an expandable needle electrode (Starburst, 2–3 cm, or Starburst XL, 3–5 cm). With the Radionics device, treatment involved either a cluster (three-prong, 2.5 cm active tip) or a single (2 or 3 cm active tip) needle electrode, depending on the size of the tumor. Each tumor received one to four ablations in one session. The number of ablations performed in one session was based on the size of the tumor.

Imaging assessment

After RFA, all patients underwent immediate follow-up US or contrast-enhanced dynamic computed tomography (CT) to evaluate the possibility of bleeding or fluid accumulation. The efficacy of RFA was evaluated using contrast-enhanced dynamic CT 1 month after treatment and then every 3 months. Treated tumors were assessed for residual tumor and size changes. All follow-up images were also assessed for the development of new metastatic disease and ancillary peritumoral changes.

Residual disease was defined as persistent tumor without necrosis in an area or areas after ablation, as determined at the 1-month follow-up study. Recurrent disease was defined as new tumor development after at least one imaging study had demonstrated complete eradication of tumor. Assessment of images was performed in consensus by three experienced radiologists (YYC, YHC, and Jen-Huey Chiang).

Table. Demographic data of 10 patients with intrahepatic cholangiocarcinoma

Age (yr)	Gender	Location	Size (cm)	Viable tumor	Pre-RFA		Post-RFA	
					CEA*	CA19-9*	CEA	CA19-9
71	M	S2	2.2	No	0.8	12.2	1.6	13.2
63	F	S4	1.9	No	2.4	16.9	3.0	14.2
38	F	S4	5.1	No	7.6	28.3	3.8	24.0
75	F	S2–3	4.6	Yes	2.8	73.2	2.7	56.6
86	M	S6	2.4	No	ND	ND	ND	ND
59	F	S6–7	6.8	Yes	22.4	86.3	14.0	42.7
73	M	S5	2.3	No	ND	ND	1.0	9.8
63	M	S7	3.1	No	ND	ND	ND	ND
67	M	S7	2.5	No	5.9	26.4	3.2	16.1
73	M	S8	3.5	No	ND	ND	1.8	11.7

*Normal range: carcinoembryonic antigen (CEA) < 6.00 ng/mL; CA19-9 < 34.60 U/mL. ND = no available data.

RESULTS

There were 12 sessions of RFA for 10 solid hepatic tumors in 10 patients. Eight patients were treated at a single session and the other two had two treatment sessions. Six tumors were located in the left hepatic lobe and four in the right hepatic lobe. Four patients were treated with the RITA device and six with the Radionics device. Of the patients treated with the RITA system, one was treated with the 2–3 cm active electrode and three were treated with the 3–5 cm active electrode. Of the patients treated with the Radionics system, one was treated with the 2 cm active tip electrode, four with the 3 cm active tip electrode, and one with the 2.5 cm cluster electrode.

The duration of follow-up ranged from 4 to 38 months (mean, 20 months). Post-treatment CT showed total necrosis in eight of 10 tumors (80%) after one or two sessions of RFA (Figure). Residual tumor was observed in two patients with larger tumors (4.6 and 6.8 cm in diameter). One of these two patients died 14 months after percutaneous RFA. Complete necrosis was seen in all five tumors (100%) with diameters of 3.0 cm or less, two of three tumors (75%) with diameters of 3.1–5.0 cm, and one of two tumors (50%) larger than 5.0 cm. One recurrent tumor was found 16 months later in one patient with complete necrosis.

All patients tolerated the procedure with no major complications. One patient had a large biloma after the procedure, which resolved after 6 months with percutaneous drainage. Two patients had low-grade fever ($< 38.5^{\circ}\text{C}$), which resolved in 1 week without antibiotic treatment. Two patients had pain or paresthesia around the puncture site for several days after the procedure, which resolved spontaneously in 2 and 4 weeks, respectively. All patients received a prescription for pain medication (acetaminophen or a non-steroidal anti-inflammatory drug) for 3–5 days on discharge from hospital. No patient experienced the postablative pain syndrome (pain, fever, malaise, and leukocytosis) described after hepatic RFA, and no patient received antibiotics before, during, or after the procedure.

DISCUSSION

Percutaneous RFA has been successfully used to treat liver neoplasms [4–8,11,12]. Radiofrequency thermal ablation works by converting radiofrequency waves into heat through ionic vibration. Alternating current passing from an electrode into the surrounding tissue causes ions to vibrate in an attempt to follow the change in the direction of

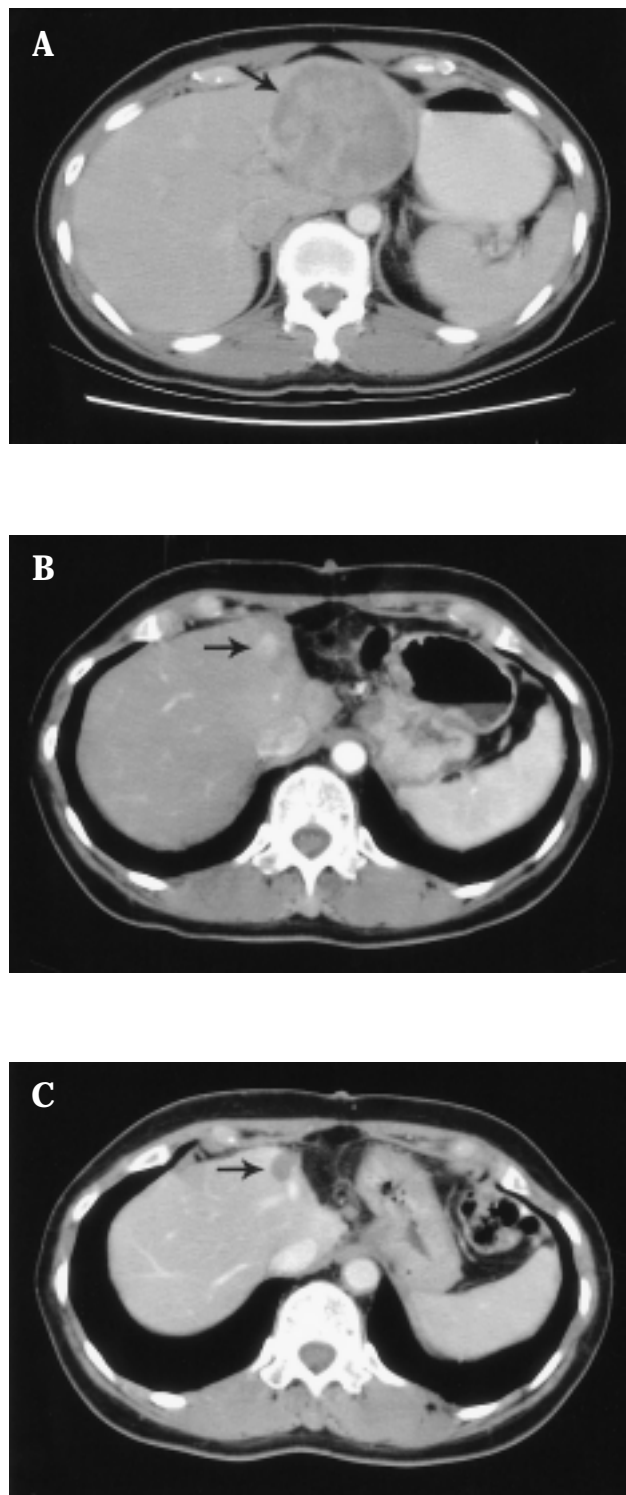


Figure. A 63-year-old woman with biopsy-proven recurrent cholangiocarcinoma in S4 of the left hepatic lobe. (A) Computed tomography (CT) before surgery shows a 5 cm heterogeneous enhancing soft-tissue mass (arrow) in the lateral segment of the left hepatic lobe. (B) Unfortunately, 1 year after segmentectomy of the lateral segment, a 2 cm recurrent cholangiocarcinoma (arrow) is evident in S4 of the left hepatic lobe. (C) CT 10 months after percutaneous ultrasound-guided radiofrequency ablation shows no enhancement of the nodule (arrow).

the rapidly alternating current. It is the ionic friction that generates heat within the tissue and not the electrode itself. The higher the current, the more vigorous the motion of the ions and the higher the temperature reached over a period of time, eventually leading to coagulation necrosis and cell death. The purpose of RFA is to achieve local temperatures that are lethal to the targeted tissue. Generally, thermal damage to cells begins at 42°C; above 60°C, intracellular proteins are denatured, the lipid layer melts, and irreversible cell death occurs [13,14].

Although cholangiocarcinoma is generally considered to be slow growing, surgical resection offers the best opportunity for improving long-term survival. Chemotherapy and radiation have produced mixed results and are considered adjunct treatments to surgical resection [15,16]. Intraluminal brachytherapy has been used within transhepatic biliary stents for cholangiocarcinoma, but post-treatment survival has generally been poor [15,17,18].

The traditional treatment for localized intrahepatic cholangiocarcinoma is surgical resection [18], but this method is not ideal for all tumors because some patients are unable or unwilling to undergo surgery or have limited functioning hepatic tissue [19]. Attention has recently focused on RFA as a minimally invasive treatment option for hepatic neoplasms, and various outcomes have been reported [14–18,20]. The length of hospital stay, treatment cost, and risk of complications tend to be less with RFA than surgery.

The success rate of RFA in treating primary and metastatic hepatic tumors is largely dependent on tumor size [15,17,18]. In our study, no tumors smaller than 3 cm had residual or recurrent tumor on follow-up CT scans. Residual tumor was found in the two patients with tumors greater than 5 cm after a single session of RFA, and was still detected in one patient after a second session of RFA. This suggests that larger tumors are more difficult to completely eradicate with RFA. Other factors that may affect the success rate of RFA are tumor location and surrounding tissue. Centrally located tumors are more difficult to treat successfully as a result of heat loss caused by the extensive vascularity in the hepatic hilum. During RFA, heat loss occurs at the needle tip mainly through convection by means of blood circulation [13,14]. On the other hand, surrounding fibrosis, as seen in cirrhotic patients [20], is expected to reduce thermal conduction and heat dissipation, thus improving the treatment effect.

A major advantage of RFA is the ability to avoid tract bleeding and tumor seeding by coagulating the puncture tract during electrode withdrawal. No hematoma or tumor seeding after RFA was found in our study. The rate of serious complications after RFA is low. Some studies show that RFA of

primary or metastatic hepatic tumors has a low complication rate, around 4.6–13.1% [21–23]. One of our 10 patients (10%) had a serious complication: a large biloma developed after RFA, but it was totally resolved after 6 months with percutaneous drainage. Two patients had local pain or paresthesia around the puncture site for several days or weeks, which subsided spontaneously. This, presumably, was due to transient damage to the intercostal or lumbar nerves in the affected dermatome. Two patients had transient low-grade fever after RFA, which resolved with oral analgesics. Other reported complications are abscess, pneumothorax, peritoneal hemorrhage, and acute cholecystitis, all of which can be treated conservatively [21,22].

One limitation of our study is that the outcome of RFA was judged by contrast enhancement on follow-up CT scan, with a lack of enhancement implying that no viable tumor remained. Lack of enhancement on follow-up imaging has generally been assumed to mean lack of viable tumor [19]. If the tumors were hypovascular on CT studies before RFA, we measured the density of the whole necrotic area after RFA to determine if there remained persistent viable tumor. From our experience, it is crucial to choose an ablation protocol and RFA electrode that can create a necrosis zone large enough to achieve a sufficient safety margin. We believe that lack of contrast enhancement on CT indicates complete tumor eradication, but follow-up surveillance imaging is warranted because long-term results of RFA for cholangiocarcinoma are lacking, and later scans should be used to detect local or metastatic lesions.

In conclusion, percutaneous US-guided RFA is a technique of rapidly increasing usefulness. It allows safe and effective treatment of hepatic tumors. As a minimally invasive procedure, it is ideally suited for patients who are not good surgical candidates. The success of RFA for intrahepatic cholangiocarcinoma was primarily influenced by the size of the tumor. RFA is a very promising technique that is most successful in treating intrahepatic cholangiocarcinoma smaller than 3 cm, and satisfactory in treating tumors between 3 and 5 cm. Long-term follow-up data regarding local and systemic recurrence and survival are still needed, and will provide additional guidelines for the most appropriate selection of patients suitable for this treatment.

REFERENCES

1. De Vreede I, Steers JL, Burch PA, et al. Prolonged disease-free survival after orthotopic liver transplantation plus adjuvant chemoradiation for cholangiocarcinoma. *Liver Transpl* 2000; 6:309–16.

2. Lillemoe KD, Cameron JL. Surgery for hilar cholangiocarcinoma: the Johns Hopkins approach. *J Hepatobiliary Pancreat Surg* 2000;7:115-21.
3. Reed D, Vitale G, Martin R, et al. Bile duct carcinoma: trends in treatment in the nineties. *Am Surg* 2000;66:714-5.
4. Livraghi T, Goldberg SN, Lazzaroni S, et al. Small hepatocellular carcinoma: treatment with radio-frequency ablation versus ethanol injection. *Radiology* 1999;210:655-61.
5. Lencioni RA, Allgaier HP, Cioni D, et al. Small hepatocellular carcinoma in cirrhosis: randomized comparison of radio-frequency thermal ablation versus percutaneous ethanol injection. *Radiology* 2003;228:235-40.
6. McGahana JP, Dodd GD 3rd. Radiofrequency ablation of the liver: current status. *AJR Am J Roentgenol* 2001;176:3-16.
7. Solbiati I, Goldberg SN, Ierace T, et al. Hepatic metastases: percutaneous radio-frequency ablation with cooled-tip electrodes. *Radiology* 1997;205:367-73.
8. Oshowo A, Gillams A, Harrison E, et al. Comparison of resection and radiofrequency ablation for treatment of solitary colorectal liver metastases. *Br J Surg* 2003;90:1240-3.
9. Rossi S, Di Stasi M, Buscarini E, et al. Percutaneous RF interstitial thermal ablation in the treatment of hepatic cancer. *AJR Am J Roentgenol* 1996;167:759-68.
10. Scudamore C. Volumetric radiofrequency ablation: technical consideration. *Cancer J* 2000;6:316-8.
11. Dodd GD 3rd, Soulen MC, Kane RA, et al. Minimally invasive treatment of malignant hepatic tumors: at the threshold of a major breakthrough. *Radiographics* 2000;20:9-27.
12. Ahmed M, Goldberg SN. Thermal ablation therapy for hepatocellular carcinoma. *J Vasc Interv Radiol* 2002;13:231-44.
13. Goldberg SN, Gazelle GS, Mueller PR. Thermal ablation therapy for focal malignancy: a unified approach to underlying principles, techniques, and diagnostic imaging guidance. *AJR Am J Roentgenol* 2000;174:323-31.
14. Goldberg SN, Hahn PF, Tanabe KK, et al. Percutaneous radio-frequency tissue ablation: does perfusion-mediated tissue cooling limit coagulation necrosis? *J Vasc Interv Radiol* 1998;9:101-11.
15. Hejna M, Pruckmayer M, Raderer M. The role of chemotherapy and radiation in the management of biliary cancer: a review of the literature. *Eur J Cancer* 1998;34:977-86.
16. Whittington R, Neuberg D, Tester W, et al. Protracted intravenous fluorouracil infusion with radiation therapy in the management of localized pancreaticobiliary carcinoma: a phase I Eastern Cooperative Oncology Group Trial. *J Clin Oncol* 1995;13:227-32.
17. Alden M, Mohiuddin M. The impact of radiation dose in combined external beam and intraluminal Ir-192 brachytherapy for bile duct cancer. *Int J Radiat Oncol Biol Phys* 1994;28:945-51.
18. Foo M, Gunderson L, Bender C, Buskirk S. External radiation therapy and transcatheter iridium in the treatment of extrahepatic bile duct carcinoma. *Int J Radiat Oncol Biol Phys* 1997;39:929-35.
19. Lim HK, Choi D, Lee WJ, et al. Hepatocellular carcinoma treated with percutaneous radio-frequency ablation: evaluation with follow-up multiphase helical CT. *Radiology* 2001;221:447-54.
20. Curley SA, Izzo F, Ellis LM, et al. Radiofrequency ablation of hepatocellular cancer in 110 patients with cirrhosis. *Ann Surg* 2000;232:381-91.
21. Poon RT, Ng KK, Lam CM, et al. Learning curve for radiofrequency ablation of liver tumors: prospective analysis of initial 100 patients in a tertiary institution. *Ann Surg* 2004;239:441-9.
22. Curley SA, Marra P, Beaty K, et al. Early and late complications after radiofrequency ablation of malignant liver tumors in 608 patients. *Ann Surg* 2004;239:450-8.
23. Shankar S, vanSonnenberg E, Silverman SG, et al. Diagnosis and treatment of intrahepatic biloma complicating radiofrequency ablation of hepatic metastases. *AJR Am J Roentgenol* 2003;181:475-7.

超音波導引下經皮熱射頻滅除術治療肝內膽管癌

邱怡友^{1,3} 黃振義^{2,3} 周宜宏^{1,3} 王信凱^{1,3} 姜仁惠^{1,3} 張政彥^{1,3}

¹台北榮民總醫院 放射線部 ²台中榮民總醫院 放射線部

³國立陽明大學 醫學院

本研究是評估超音波導引下經皮熱射頻滅除術治療肝內膽管癌的臨床應用、治療效果，以及併發症。從 2002 年 1 月到 2004 年 10 月，共有 10 位病理診斷為肝內膽管癌的病人，接受了超音波導引下經皮熱射頻滅除術治療腫瘤。這些病人 (6 位男性與 4 位女性) 的平均年齡是 66.2 歲 (年齡範圍為 38 歲到 86 歲)。腫瘤的大小平均是 3.4 公分 (範圍 1.9 到 6.8 公分)。治療完後一個月以動態電腦攝影評估其效果，然後每隔 3 個月追蹤一次。有 6 個病人是使用內冷卻式的 Radionics 探針，另外 4 個病人是使用可擴張性的 RITA 探針。電腦斷層掃描檢查時注射顯影劑後腫瘤沒有顯影，則表示腫瘤已經壞死。這 10 位病人 (10 個腫瘤) 共接受了 12 次的治療，8 位病人接受 1 次治療，2 位病人接受 2 次治療。治療後動態電腦攝影顯示 8 位病人的腫瘤完全壞死。以腫瘤大小來評估其效果，小於 3 公分的腫瘤有 5 位，腫瘤完全壞死率是 100%，3 到 5 公分有 3 位，腫瘤完全壞死率 67%，大於 5 公分的有 2 位，腫瘤完全壞死率 50%。1 位病人術後發生膽汁聚積的情形，經過引流，6 個月後已完全消失。總之，經皮熱射頻滅除術可以有效的治療肝內膽管癌，尤其是小於 3 公分的腫瘤，對於 3 到 5 公分腫瘤的療效也很不錯，治療後併發症的比例也很低。

關鍵詞：肝內膽管癌，肝臟，腫瘤，熱射頻滅除術

(高雄醫誌 2005;21:304-9)

收文日期：94 年 3 月 3 日

接受刊載：94 年 5 月 13 日

通訊作者：周宜宏醫師

台北榮民總醫院放射線部

台北市 112 石牌路 2 段 201 號