

Complete ablation rate of percutaneous radiofrequency ablation of hepatocellular carcinoma in favorable and unfavorable locations: using real time ultrasound guidance and expandable electrode needle

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Objective To evaluate the success rate of percutaneous radiofrequency ablation (RFA) for hepatocellular carcinoma (HCC) by using real time ultrasound guidance and expandable electrode.

Methods A retrospective study reviewed of CT and MRI findings from August 2015 to October 2016 of 91 HCCs. The patient's data, RFA data, location of the HCC, complication after procedure and imaging success rate of complete ablation were analyzed. The size of tumor range 0.5-4.5 cm. We performed RFA by using real time ultrasound guidance and expandable electrode needle (LeVeen, Boston scientific cooperation, USA) with stepwise method and double ablation method to reduce ablation time and more ablative area. The unfavorable locations of tumor (exophytic appearance, near capsule, near gallbladder, near bowel, near vessels) were performed without artificial ascites.

Results Complete ablation was obtained in 91.2% (83/91) of all HCCs. The complete ablation rate in favorable location was 100% (12/12), while the complete ablation rate in unfavorable location was 89.9% (71/79). Only one complication was found in 91 sessions of all HCCs.

Conclusion Using expandable electrode catheter combined with real time ultrasound guidance help ablates tumor in high risk locations with high success rate, low complication and fast operation time. **Chiang Mai Medical Journal 2018;57(1):1-9.**

Keywords: radiofrequency ablation, unfavorable location, hepatocellular carcinoma

Introduction

Worldwide, hepatocellular carcinoma (HCC) is the fifth most common malignancy in men and the eighth in women (1). HCC is also the most common type of liver cancer worldwide in both men and women, with the majority of cases occurring in patients with cirrhosis of the liver. It is known to be associated with hepatitis B and C infections (2). In Thailand, liver cancer is the

third leading cause of death from malignant neoplasms in males, following lung and stomach cancer. In females, liver cancer ranked fifth as a cause of death during the past decade, following colon, stomach, lung, and breast cancer (3). The diagnosis and staging of HCC in this study followed the American Association for the Study of Liver Diseases (AASLD) and the Barcelona

Clinic Liver Cancer (BCLC) guidelines (4).

There are several options that provide a high rate of complete response. These include surgical resection, liver transplantation, and percutaneous techniques of tumor ablation (5). The only definitive treatment modalities capable of achieving a cure are hepatic resection and hepatic transplantation. Most patients, however, are not candidates for these therapies (6). As a result, percutaneous ablation plays a key role in the therapeutic management of HCC (7). Ultrasoundography (US)-guided radiofrequency ablation (RFA) is an effective, fast, and real-time targeting modality for small HCCs (4). Often tumors are found in difficult locations (e.g., abutting key structures such as the bowel, gallbladder, diaphragm, liver capsule, large blood vessels, and exophytic locations) that may be injured during RFA or where an insufficient ablation safety margin might result in residual tumor. Many recent studies have reported that new technologies are leading to achieving improved tumor necrosis rates and reduced complications with RFA treatment in such tumors. The purpose of this retrospective study is to evaluate the success rate of percutaneous radiofrequency ablation of hepatocellular carcinoma and complications following the procedure.

Methods

Patients

This study was approved by the institutional review board; the informed consent requirement was waived because this is a retrospective clinical study. The radiofrequency ablation record database from Maharaj Nakhon Chiang Mai hospital from August 2015 to through October 2016 revealed that 107 liver tumors had been

performed using radiofrequency ablation. We included only patients who had been diagnosed with hepatocellular carcinoma according to AASLD guidelines and who had undergone percutaneous radiofrequency ablation. All tumors showed arterial hypervascularity and portal or delayed washout and were less than 3 cm in size. Other inclusion criteria included computed tomography (CT) or magnetic resonance imaging (MRI) done within 3 months before and again 3 months after the procedure. Sixteen patients were excluded from the study: 1 patient did not have pre-operative images, 7 patients did not have follow up images, 5 patients were not diagnosed with HCC, and 3 patients were performed on non-targeted lesions. A total of 73 patients with 91 nodules were included in the study.

The ablative technique

Real time ultrasound guidance, (iSTYLE, Toshiba, Japan) was used and the patients were admitted to hospital. An anesthesiologist was consulted for intravenous sedation and pain control during the procedures. All procedures were performed by two interventional radiologists with 5 and 6 years experience.

All patients received radiofrequency ablation using multi-tined expandable electrodes (LeVeen Needle Electrodes, Boston Scientific Cooperation, U.S.A.) (Figure 1), size 2 to 4 cm in combination with an RF 3,000 generator (Boston Scientific Cooperation, U.S.A.) (Figure 2).

The needle was inserted into the target location. As a first step, the tines were expanded to 1 cm, and current was delivered until power rolloff occurred. Using 1 cm stepwise expansion of the tines, ablation was repeated until the tines were fully expanded. RF energy was applied with an initial power setting of 20W. The electrical power was increased by 10W every 30 seconds until rolloff. The initial electrical power for 2 cm, 3 cm, 3.5 cm and 4 cm expanded tines were 30W,



Figure 1. Multi-tined expandable electrode (LeVeen electrode needle Needle Electrodes, Boston Scientific Cooperation, U.S.A.)



Figure 2. RF 3,000 generator (Boston Scientific Cooperation, U.S.A.)

40W, 50W and 80W, respectively.

We also used the double ablation method (DAM) with all lesions. After ablation with fully expanded tines had been performed, the needle was moved back 1 to 2 cm and stepwise ablation was performed again (Figure 3). In high risk areas such as near the gallbladder or exophytic locations, the tines were expanded carefully.

Data evaluation

All CT and MR images were reviewed on a picture archiving and communication system (PACS) using a Synapse version 4.1 workstation. One interventionist evaluated the CT and MRI findings for each parameter.

Pre-operative CT/MRI were evaluated for tumor size, site of the HCC including location of the hepatic lobe, exophytic appearance, location of nearby blood vessels, liver Glisson's capsule, gallbladder, bowel and other organs. Residual tumor and complications such as liver abscess, abdominal wall abscess, duct dilatation, perihepatic hematoma, fistula, perforation, and pleural effusion were evaluated in follow-up images.

Tumor size and size of the ablative zone were defined as the maximum axial diameter in the follow up CT/MRI 4 weeks after treatment. Location of the hepatic lobe was classified as right hepatic lobe, left hepatic lobe, or caudate lobe by the Couinaud classification. An exophytic location was defined as having more than 50% of the tumor located beyond the hepatic capsule. Location near an organ was defined as within 10 mm of an organ. Vessels equal to or greater than 3 mm were used for evaluation.

Complications from radiofrequency ablation were defined as a change in imaging between pre-operative and follow-up images. Complications visible in pre-operative images were not included in the evaluations. Residual unablated tumors were evaluated following AASLD guidelines.

Statistical analysis

All statistical analyses were performed with the SPSS statistical package version 17.0. Continuous data were expressed as median and range.

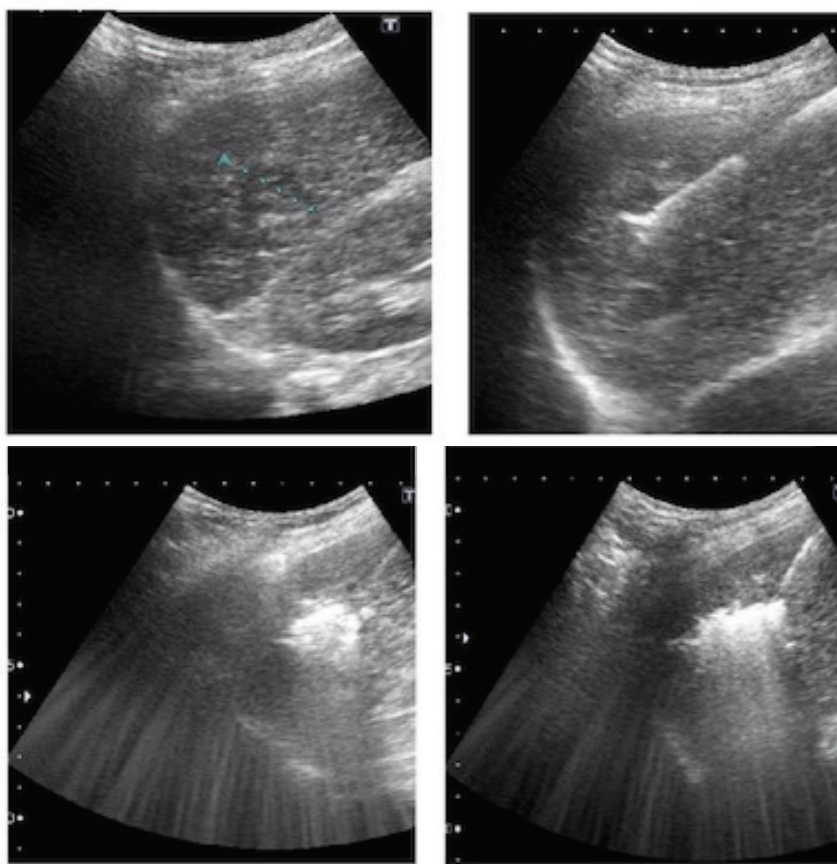


Figure 3. Radiofrequency ablation of hepatocellular carcinoma using the double ablation method (DAM) with stepwise ablation.

Results

Demographic data

The study included 73 patients (62 males and 11 females) with a total of 91 tumors. The mean age of the patients with imaging diagnosis of hepatocellular carcinoma was 59.99 years (range 32-85). Most tumors were located in the right hepatic lobe followed by left hepatic lobe and the caudate lobe. The size of tumors ranged from 0.50 to 4.50 cm with a mean size of approximately 1.56 cm.

Characterization of tumor locations

Locations of tumors is summarized in Table 1. Locations of the tumors were divided into two major subgroups, favorable and unfavorable locations. Of the 91 liver tumors, 12 tumors (13.2%) were located in a favorable location and the remaining 79 tumors (86.8%) were in unfavorable locations. Unfavorable locations were subdivided into exophytic appearance (5 tumors or 5.5%), near capsule (59 tumors or 64.8%), near vessel (45 tumors or 49.5%), near gallbladder (7 tumors or 7.7%) and near bowel (13 tumors or 14.3%) (Figure 4). One tumor could belong to more than one unfavorable location subgroup.

Comparison of success rates of ablated lesions

Most of the ablated lesions showed com-

Table 1. Tumors characteristics

Tumors	(n=91)
Tumor size, cm	1.56
Location	
Left lobe	26 (28.6%)
Caudate lobe	4 (14.4%)
Unfavorable locations	
Exophytic appearance	5 (5.5%)
Near liver capsule	59 (64.8%)
Near vessel	45 (49.5%)
Near gallbladder	7 (7.7%)
Near bowel	13 (14.3%)

plete necrosis. Only 8 liver tumors had residual unablated tumors. The success rate for complete necrosis was 91.2%. The 8 incomplete ablative lesions (Figure 5) were characterized as 2 exophytic appearance, 5 near capsule, 5 near vessel, 2 near gallbladder, and 1 near bowel. Of the remaining 83 completed necrosis tumors (Figure 6), 12 were located in a favorable location and 71 in an unfavorable location. The unfavorable locations of complete necrosis tumors were subdivided into exophytic appearance (3 tumors), near capsule (54 tumors), near vessel (40 tumors), near gallbladder (5 tumors) and near bowel (12 tumors).

The average size of incomplete ablation tumors and complete necrosis tumors were 2.06 cm (range 1.10 to 4.50 cm) and 1.51 cm

Table 2. Comparison of characteristics of incomplete ablation tumors and complete necrosis tumors

Characteristics	Incomplete ablation tumors (n=8)			Complete necrosis tumors (n=83)		
Favorable location	0 (0)			12 (14.5%)		
Exophytic appearance	2 (25%)			3 (3.6%)		
Near capsule	5 (62.5%)			54 (65.1%)		
Near vessel	5 (62.5%)			40 (48.2%)		
Near gallbladder	2 (25%)			5 (6%)		
Near bowel	1 (12.5%)			12 (14.5%)		
Complications	0 (0%)			1 (1.3%)		
	Mean (cm)	Min (cm)	Max (cm)	Mean (cm)	Min (cm)	Max (cm)
Tumor size	2.06	1.10	4.50	1.51	0.50	3.50
Needle size	3.25	2.00	4.00	3.13	2.00	4.00
Ablative zone	3.13	2.10	6.00	2.77	0.98	4.80
Ablation time	7.29 min	1.29 min	21.08 min	10.36 min	0.48 min	71.45 min

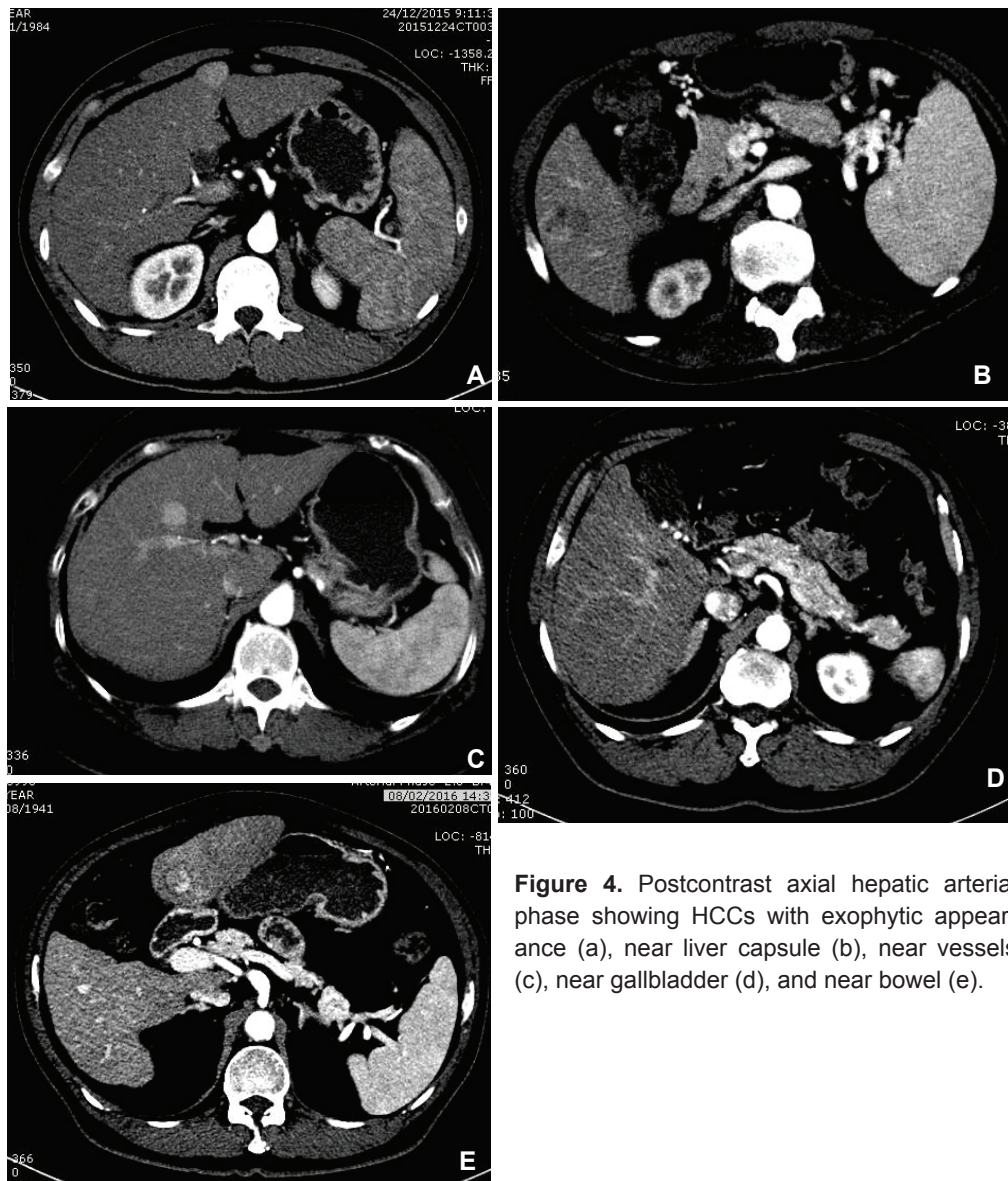


Figure 4. Postcontrast axial hepatic arterial phase showing HCCs with exophytic appearance (a), near liver capsule (b), near vessels (c), near gallbladder (d), and near bowel (e).

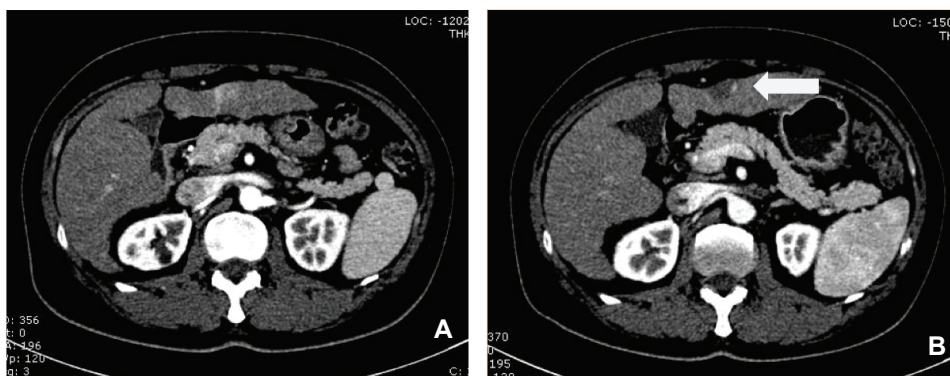


Figure 5. Postcontrast axial hepatic arterial phase of hepatocellular carcinoma in a 65-year-old man before (a) and 2 months after RFA (b) showing incomplete ablation with arterial enhancement at the left lateral portion of the RFA site (arrow) indicating residual tumor.

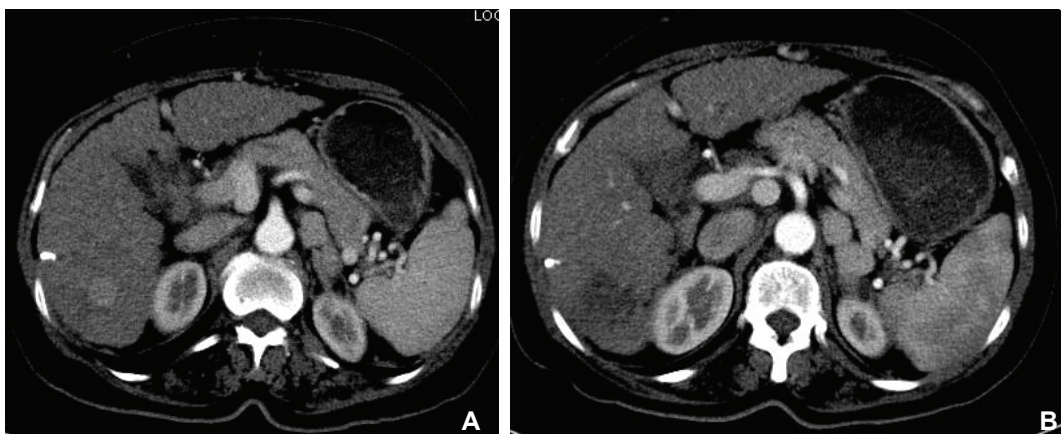


Figure 6. Postcontrast axial hepatic arterial phase of hepatocellular carcinoma in a 69 year old woman before (a) and 2 months after RFA (b) showing complete ablation without gross arterial enhancement at the RFA site.

(range 0.50 to 3.50 cm), respectively. The average needle size used with incomplete ablation tumors and complete necrosis tumors was 3.25 cm and 3.13 cm, respectively (range 2.00 to 4.00 cm). The average ablative zone of incomplete ablation tumors and complete necrosis tumors was 3.13 cm (range 2.10 to 6.00 cm) and 2.77 cm (range 0.98 to 4.80 cm), respectively. The average ablation time for incomplete ablation tumors and complete necrosis tumors was 7.29 minutes (range 1.29 to 21.08) and 10.36 minutes (range 0.48 to 71.45), respectively. There was 1 complication, an abdominal wall abscess, which occurred in a complete necrosis tumor. Comparison of incomplete ablation tumors and complete necrosis tumors is shown in Table 3.

Comparison of tumor location parameters

Overall, tumor size was smaller in favorable locations (1.30 vs. 1.60 cm). Average needle size in favorable and unfavorable locations

was approximately 3.12 cm and 3.15 cm, respectively. The average ablation time and ablative zone of favorable locations was about 9.88 minutes and 3.05 cm, while for unfavorable locations the values were about 10.12 minutes and 2.77 cm. With tumors in unfavorable locations, the complication rate was 1.3% (1 case) and the success rate was 89.9%. Comparison between favorable and unfavorable locations are shown on Table 3.

Discussion

Although surgical resection is the gold standard treatment for hepatic tumors, particularly primary tumors, there is a small group that can performed surgery (6).

Percutaneous ablation is safe and should be considered the best treatment option for patients with early-stage HCC who are not candidates for surgical resection or liver transplantation (8-11).

Table 3. Comparison of tumors in favorable and unfavorable locations

Characteristics	Favorable location (n=12)			Unfavorable location (n=79)		
	Mean (cm)	Min (cm)	Max (cm)	Mean (cm)	Min (cm)	Max (cm)
Tumor size	1.30	0.74	1.90	1.60	0.50	4.50
Needle size	3.12	2.00	4.00	3.15	2.00	4.00
Ablative zone	3.05	0.98	4.30	2.77	1.43	6.00
Ablation time	9.88 min	3.55 min	27.64 min	10.12 min	6.48 min	71.45 min
Complications		0%			1.3%	
Complete necrosis		100%			100%	

Huang *et al.* reported a randomized trial comparing RFA and surgical resection for HCC conforming to the Milan criteria with 1-, 2-, 3-, 4- and 5-year overall survival rates for the RFA group and the resection group of 87%, 77%, 70%, 66%, 55%, and 98%, 97%, 92%, 83%, 76%, respectively (12).

Recent prospective randomized trials have concluded that percutaneous RFA is as effective as surgical resection for small HCCs. Complete ablation rates after a single session of radiofrequency ablation of HCC vary from 48% to 97% (13). Vincent Wai-To Lam reported 91.6% complete tumor ablation and found that incomplete ablation (8.4%) was associated with tumors larger than 3 cm, pre-operative serum alpha fetoprotein more than 200 ng/ml, and nodules located in an area difficult to ablate (14). In our study, the overall complete ablation rate was 91.2% (73 of 91). The success rate of percutaneous RFA in our study was not different from previous studies (6, 13, 15, 16).

A limitation of RFA is its susceptibility to cooling from blood flow in adjacent blood vessels, the heat-sink effect (17). Thanos *et al.* reported a 79% complete ablation rate for tumors in contact with a blood vessel more than 3 mm in diameter (18). In our study, the complete ablation rate in nodules close to a portal vein was 88.9%. This result suggests that tumors close to a vessel have a higher incomplete ablation rate.

Another factor related to incomplete ablation is location in a difficult area, e.g., in the caudate lobe, near the intestine, in a subcapsular location, and tumors with an exophytic appearance (19). In our study, the complete ablation rate of tumors in an unfavorable location was 89.9%. This is comparable to a study by Zhe Tang *et al.* from China which evaluated the feasibility of ultrasound guided RFA for hepatic tumors in high-risk areas (close to a portal vein, the inferior vena cava, a bile duct, the gallbladder, the stomach, the intestine or the diaphragm) which reported a complete ablation rate of 89.0%.

There are a few methods, such as artificial ascites or pleural effusion, which can help improve the efficacy of percutaneous radiofre-

quency ablation of hepatocellular carcinomas located on the liver surface and in the hepatic dome (20). In this study we did not perform artificial ascites or pleural effusion because of the additional ablation time required. We used an expandable electrode for adjusting the ablation size in conjunction with real-time ultrasound guidance to view images during the entire procedure. We also used the multistep method and the double ablation method which are useful for reducing ablation time with an extensive ablative zone (21, 22).

The RFA procedure involves some risk in dangerous zones. There have been two studies of percutaneous RFA in high risk and challenging locations (19, 23). We had a complication rate of only 1.3% compared to 9.5% in a study by Kelogrigoris *et al.* We found one abdominal wall abscess lesion located near the abdominal wall. We thought the abscess could have been the result of an infected hematoma. That correlates with other studies which have found subcapsular hematomas in about 4.75% of cases. In this patient, the complication did not require any surgical management.

Conclusions

RFA is a safe and effective procedure for treatment of liver tumors. Using an expandable electrode catheter combined with real time ultrasound guidance helps with ablation of tumors in high risk locations (caudate lobe, near vessels, the subcapsular region, or near an organ) and has a high success rate, low incidence of complications and shorter ablation time.

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ความสำเร็จของการรักษาผู้ป่วยมะเร็งตับด้วยการจี้ด้วยคลื่นความถี่วิทยุ

นครินทร์ อินมุตโต, ธนพ ศรีสุวรรณ, ธเนศ ชัตติพัฒนาพงษ์ และ ชินณุ เก้าวรกาญจน์
ภาควิชารังสีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ เพื่อประเมินความสำเร็จของการรักษาผู้ป่วยมะเร็งตับด้วยการจี้ด้วยคลื่นความถี่วิทยุโดยใช้เครื่องตรวจด้วยคลื่นเสียงความถี่สูงร่วมกับเข็มจี้ไฟฟ้าที่สามารถปรับขนาดได้

วิธีการศึกษา การศึกษาข้อมูลย้อนหลังภาพถ่ายมะเร็งตับจำนวน 91 ภาพ จากข้อมูลภาพถ่ายเอกซเรย์ด้วยระบบคอมพิวเตอร์และภาพถ่ายจากคลื่นแม่เหล็กไฟฟ้าตั้งแต่เดือนสิงหาคม พ.ศ. 2558 ถึง เดือนตุลาคม พ.ศ. 2559 ข้อมูลที่ได้นำมาใช้วิเคราะห์ประกอบด้วย ข้อมูลเบื้องต้นของผู้ป่วย ข้อมูลการจี้ด้วยคลื่นความถี่วิทยุ ตำแหน่งของมะเร็งตับ ผลแทรกซ้อนจากการจี้ด้วยคลื่นความถี่วิทยุ และความสำเร็จของการรักษาผู้ป่วยมะเร็งตับด้วยการจี้ด้วยคลื่นความถี่วิทยุจากภาพถ่ายเอกซเรย์ด้วยระบบคอมพิวเตอร์และภาพถ่ายจากคลื่นแม่เหล็กไฟฟ้า ผู้วิจัยใช้การรักษาผู้ป่วยมะเร็งตับด้วยการจี้ด้วยคลื่นความถี่วิทยุโดยใช้เครื่องตรวจด้วยคลื่นเสียงความถี่สูงร่วมกับเข็มจี้ไฟฟ้าที่สามารถปรับขนาดได้ และใช้การจี้เป็นชั้น ๆ แบบสองชั้น เพื่อลดระยะเวลาในการรักษา และเพิ่มขอบเขตของการรักษา การรักษาดังกล่าวผู้วิจัยใช้รักษามะเร็งตับในตำแหน่งที่ทำการรักษาได้ยากโดยไม่ใช้วิธีการทำน้ำเทียมในช่องท้อง สำหรับมะเร็งตับในตำแหน่งที่ทำการรักษาได้ยาก เช่น ก้อนมะเร็งตับที่ยื่นออกมาจากเนื้อตับ ตำแหน่งใกล้ถุงน้ำดี ตำแหน่งใกล้ลำไส้ และตำแหน่งใกล้หลอดเลือด

ผลการศึกษา อัตราความสำเร็จของการรักษาผู้ป่วยมะเร็งตับด้วยการจี้ด้วยคลื่นความถี่วิทยุรวมร้อยละ 91.2 (83/91) อัตราความสำเร็จของการรักษาผู้ป่วยมะเร็งตับในตำแหน่งปกติรวมร้อยละ 100 (12/12) ในขณะที่อัตราความสำเร็จของการรักษาผู้ป่วยมะเร็งตับในตำแหน่งที่ทำการรักษาได้ยากรวมร้อยละ 89.9 (71/79) และพบผลแทรกซ้อนจากการจี้ด้วยคลื่นความถี่วิทยุ 1 ราย จากทั้งหมด 91 ราย

สรุปผลการศึกษา การรักษาผู้ป่วยมะเร็งตับด้วยการจี้ด้วยคลื่นความถี่วิทยุโดยใช้เครื่องตรวจด้วยคลื่นเสียงความถี่สูงร่วมกับเข็มจี้ไฟฟ้าที่สามารถปรับขนาดได้ช่วยเพิ่มความสำเร็จในการรักษา ลดผลแทรกซ้อน และรวดเร็วในการรักษาผู้ป่วยมะเร็งตับในตำแหน่งที่ทำการรักษาได้ยาก **เชียงใหม่เวชสาร 2561;57(1):1-9.**

คำสำคัญ: การจี้ด้วยคลื่นความถี่วิทยุ ตำแหน่งที่ทำการรักษาได้ยาก มะเร็งตับ