Egyptian Journal of Surgery Vol. (23), No. (1), Jan., 2004

INITIAL CLINICAL EVALUATION OF RADIOFREQUENCY THERMAL ABLATION OF LIVER TUMORS

By
Tarik Abdel Azeez Ahmad, M.D., PhD, Motasem M. Ali, M.D., Younis naguib, M.D.
Department of Surgery, El-Minia University Hospital, El-Minia, Egypt

Background: *In spite of recent advances in cancer therapy, treatment of primary and metastatic tumors of liver remains a significant challenge to the health care community worldwide. Surgical resection is considered the gold standard for treatment of liver tumors; however, the majority of patients are not candidates for surgical resection.*
Aim: *The study aims at evaluation of the role of radiofrequency ablation in the treatment of primary and metastatic liver tumors in patients who are not candidates for surgery.*
Patients and methods: *For nine months, patients with primary or metastatic liver tumors, that were excluded from surgical treatment, were subjected to radiofrequency thermal ablation. Three cases of this series were excluded due to anatomical considerations and advanced disease. The study included 35 focal lesions in 21 patients. After the lesions were identified and biopsied, they were thermally ablated. The ablation zone was evaluated by comparing preoperative triphasic CT scanning of the liver with postoperative scan obtained one month after ablation.*
Results: *The procedure was completed in all patients without complications. Twenty lesions were primary liver tumors while fifteen lesions were metastatic. The mean tumor diameter was (2.5+1.1mm) and the average number of lesions per patient was (1.67+0.7) ranging from one to three masses. Thirty-three lesions were treated with a single ablation session including overlapping technique in seven lesions while two lesions required a second session. Fifteen patients received percutaneous ablation while six patients received intraoperative ablation. The follow-up period ranged from 3 to eight months without any reported cases of recurrence; however, two new lesions appeared in two patients that were scheduled for another session of ablation.*
Conclusion: *Radiofrequency ablation offers a new safe technology that should be considered for treatment of liver tumors when surgery is not a valid option.*

INTRODUCTION

In spite of recent advances in cancer therapy, treatment of primary and metastatic tumors of liver remains a significant challenge [1]. Hepatocellular carcinoma is one of the most common malignancies and the number of patients is increasing due to the changing prevalence of hepatitis C. This disease affects one million persons every year with an overall dismal survival [2]. Surgery remains the gold standard for treatment of liver tumors in spite of being potentially curative with a five-year survival ranging from 25 to 55% [3]. Moreover, most patients are poor candidates for surgical resection and those patients who underwent surgery may suffer a recurrence [4]. Many patients with a recurrent liver tumor are not candidates for re-resection. On the other hand, both chemotherapy and irradiation have a low success rate and neither is without complications [5, 6]. For these reasons, increasing interest has been focused on ablative approaches for treatment of unresectable liver tumors [7-9]. Radiofrequency ablation (RFA) is becoming the most commonly used and perhaps the most promising modality for tumor ablation not only for liver tumors but for a wide variety of tumors as well [10, 11]. This study throws the light on initial evaluation of RFA for management of unresecable liver tumors.

PATIENTS AND METHODS

During the period from January to September 2002, a

co-study between El-Minia University and Nagasaki University included twenty-one patients suffering from focal lesions in the liver where resection was not a valid option.

Patients' selection:

To be eligible for thermal ablation therapy, patients must fulfill some general rules. First, because RFA is a local treatment, the tumor should be confined to the liver without any evidence of vascular invasion or extra-hepatic metastasis. Full clinical, laboratory and radiological evaluation is necessary to establish the indication for ablation therapy. The lesion must be either uni-nodular, or when multi-nodular, have a maximum of three to four nodules. The number of nodules stood behind exclusion of some patients with advanced multinidular focal lesions (Fig 1A) Tumor size should be ideally smaller than 3-4 cm in largest diameter. However, larger lesions can be treated with 5-cm needle and with multiple overlapping insertions technique. Treatment of lesions adjacent to the gallbladder or the hilum of the liver carries a risk of thermal injury to the biliary tract and that risk was another reason for exclusion from the study (Fig 1B). In contrast, treatment of lesions in the vicinity of hepatic vessels is possible because of the cooling effect of blood stream prevents thermal injury of the vascular wall but these cases may suffer incomplete ablation because of the heat sinking effect of the blood flow. For metastatic disease, histology and extension of the primary tumor is a determining factor for eligibility for ablation therapy. The best indication is metachronous metastasis from a gastrointestinal malignancy, especially colorectal tumors.

Technique

RFA can be performed under local anesthesia, conscious sedation or general anesthesia. Liver function is evaluated before and 24 hours after the procedure. Using a space filling technology, the RFA generator is coupled with an active expandable electrode needle that has an insulated stainless steel shaft and an exposed active tip with retractable jackhooks. The hooks can be deployed laterally and retracted manually by moving the graduated control mechanism on the handle of the needle. The catheter used in this study consists of 14-gauge needle, 25cm in length (RITA Medical Systems, Starburst XL). Once the catheter tip is positioned at the intended ablation zone, nine curved prongs are deployed that deliver radiofrequency electrical energy to the tissues. One electrode at the center and four electrodes going to the equator have thermocouples at the tips for monitoring temperature at the ablation. The power output is adjusted either manually or automatically to keep temperature between 95° and 105°. Ablation of the track with the exposed trocar tip is performed to prevent seeding of the tumor cells as well as to secure haemostasis along the track. The RFA generator can be connected to a computer that continuously records the temperature curves obtained during the treatment and provides an objective documentation of the outcome of the using RITA-Base graphic display and patient documentation software (Fig 2).

The approach to the hepatic mass can be achieved through different ways. The tumor can be ablated through percutaneous approach, open surgical approach, laparoscopic approach or recently, the thoracoscopic approach was used for lesions at the dome of the liver that used to be considered inaccessible (Fig. 3) [12].

Evaluation of the success of the procedure is obtained by a CT study that shows replacement of the tumor area with an area of necrosis matched to the original lesion. After ablation, a halo of hypervascularity is expected around the ablated lesion caused by inflammatory reaction and lasts for few days so the best time to assess the ablation therapy is one month after the procedure.

A careful follow-up protocol is to be recommended in the case of metastases treated by RFA. The recurrence of the treated lesion is more frequent in metastases than in HCC. In addition, patients with metastases are at high risk for developing new intrahepatic lesions or extrahepatic metastases.

Statistical analysis

The data are presented as a mean + S.D. The significance of differences was analyzed by Student's t–test, and a p value of < 0.05 was considered significant.

RESULTS

From January to September 2002, a series of 21 patients underwent RFA procedure for primary or metastatic tumors. The study included eight female patients and thirteen male patients and their age ranged from 49 to 72 years with an average of 58.4 + 6.7 years.

The radiological investigations showed 35 focal lesions with average number of lesions per patient of 1.67 + 0.7 ranging from one to three lesions per patient. The tumor diameter ranged from 0.7 to 4.8 mm with an average of 2.5 + 1.1 mm.

Pathological examination of the bopsies obtained from all lesions before ablation showed 20 primary lesions and 15 metastatic foci (Table 1).

A safety margin of ablated normal liver tissue is strongly recommended to ensure complete eradication of tumor cells especially for metastatic lesions; therefore, an ablation zone is measured during the follow-up radiological assessment (Fig. 4A and 4B). After one month,

the ablation zone ranged from 2.8 to 7 cm with an average of 4.63 + 1.1 cm.

Table (2) shows the outcome of the ablation sessions as regard number of sessions, needle access, recurrence or appearance of new lesions and any recorded complications of the procedure.

The changes in biochemical profile were recorded before ablation therapy then one day and one month following ablation (Table 3).

Following ablation, the patients were followed up by triphasic CT one month after RFA and every three months beside a monthly ultrasonographic evaluation that showed no recurrence; however, two new lesions appeared away from the ablated zone and they were scheduled for another session of RFA (Fig. 5).

Table (1): ***Types of Lesions included in the study***

Type of Lesions	*Number*
Primary Lesions	20
Hepatocellular carcinoma	18
Sarcoma	2
Secondary Lesions	15
Colorectal	12
Lung	3

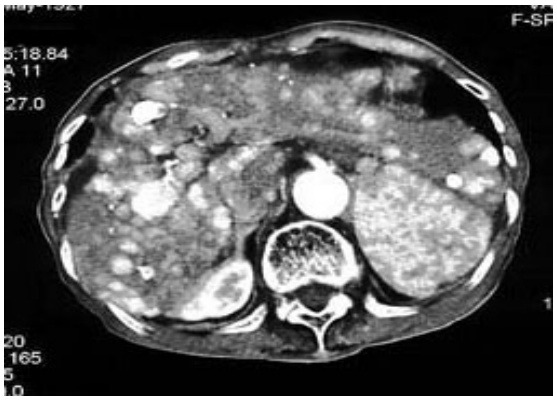
Table (2): ***Outcome of ablation series***

Outcome of ablation Series	*Number*
Single session	33
Single Insertion	26
Multipe overlapping insertion	7
Multiple Sessions	2
Access	
Percutaneous	15
Open surgery	2
Laparoscopy	2
Thoracoscopy	2
Recurrence	0
New lesions	2
Complications	
Rise in trasminases	15
Low-grade fever	6
Pain	5
Pleural effusion	2

Table (3)*: Biochemical profile*

Test	*1 day before ablation*	*1 day after ablation*	*1 month after ablation*
AST	41.1±8.4	136.2±11.8*	48.6±11
ALT	36.6±3.2	97.1±6.1#	38.1±3.9

* P<0.01 as compared to pre-ablation level.
# P<0.01 as compared to pre-ablation level.



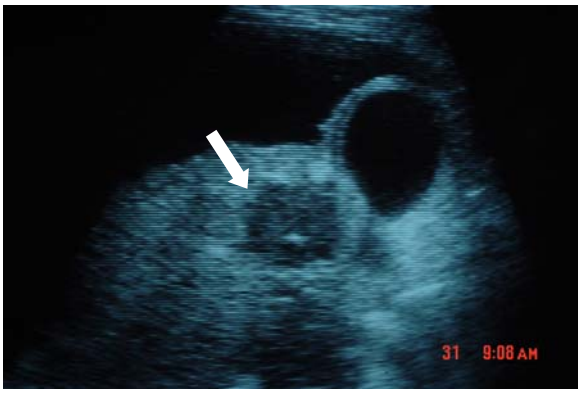


Fig. (1): This figure gives two examples of exclusion criteria. In (Fig. 1A), the CT shows multinodular advanced hepatocellular carcinoma while (Fig. 2B) shows an ultrasonographic view of a lesion adjacent to the gallbladder.

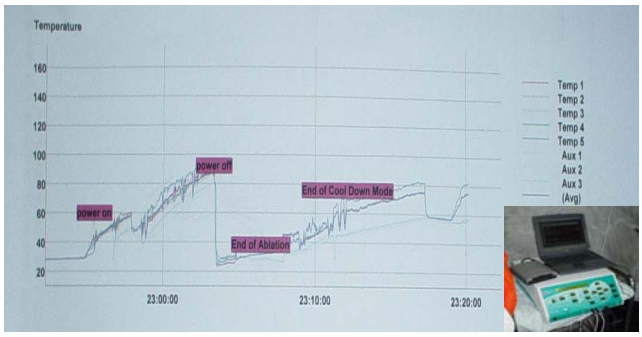


Fig. (2): Line graph shows temperature, impedance, and power profiles. The parallel lines between (power on) and (power off) indicate similar temperature in all arrays achieving the best ablation results. The lower right angle shows the device connected to a computer.

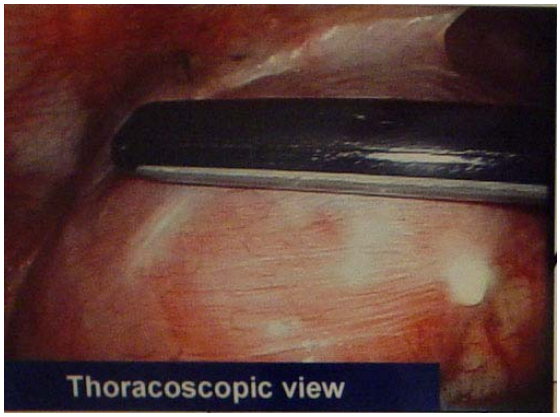
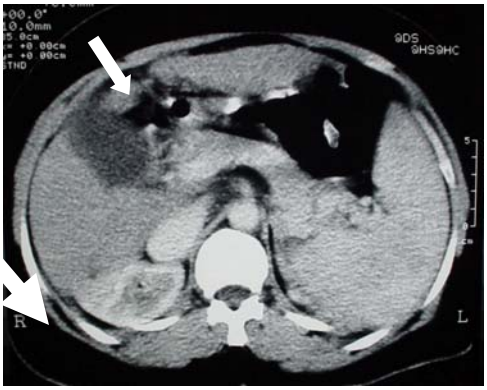


Fig. (3): Thoracoscopic view showing the diaphragm above the dome of the liver and the ultrasonographic probe used to locate the lesion.



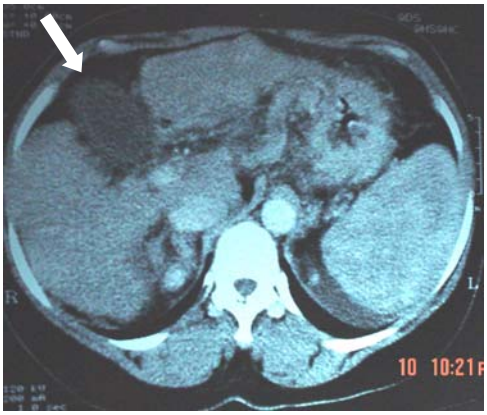


Fig.(4): (Fig. 4A) shows pre-ablation CT with the arrow pointing at an enhanced area of the lesion. In (Fig. 4B), the arrow points to the same area but without evidence of enhancement indicating success of ablation therapy.

Fig. (5): ***Ultrasonographic view after ablation where the lower arrow marks the ablated zone; however, the upper arrow points to a new lesion that appeared later.***

DISCUSSION

This study evaluated the early clinical trials of a promising modality in treatment of focal lesions of the liver in patients who are not candidates for surgery. RFA is considered mainly for focal lesions less than 5 cm with a considerable hepatic functional reserve to ensure a fruitful prognostic outcome [13]. Up to three lesions, RFA succeeded to exhibit good results on multi-focal lesions whether primary or secondary with average diameter of 2.5 cm that is in accordance with other authors' results [14- 16].

In spite of appearance of new lesions during the follow-up course, we did not experience any cases of recurrence in our series; however, other authors reported a recurrence rate of 10-12% most of which occurred mainly in larger lesions [17, 18]. Criteria of recurrence included CT changes at the ablated zone as well as appearance of new lesions encroaching on the ablated zone. Complete tumor ablation was obtained in most cases especially with the new technology and the larger needles that could achieve tumor ablation with a single insertion [19, 20].

With growing technology, a 150 watts-maximum power device replaced the old 50 watts-device and this carried a great concern of traumatizing the patient; however, the use of two grounding pads on the anterior aspects of both thighs of the patient reduced the risk to nil [21].

Percutaneous ethanol injection (PEI) emerged as a safe and effective treatment especially for nodular type HCC. The survival figures of different studies have shown that the long-term survival outcomes are almost similar for PEI and surgery. With wider use of PEI, the technique was not satisfying for larger HCC lesions or lesions with intra-tumoral septa because of incomplete diffusion of alcohol within the lesion and residual tumor tissue persisted after the procedure. In addition, PEI proved to be ineffective in the treatment of hepatic metastases, except those from endocrinal tumors. These results encouraged researchers to shift to RFA technology to ensure complete ablation or to use a combined technique employing both PEI and RA together [14-16].

Another modification to our technique was a balloon occluded RFA that showed superior results to the ordinary technique especially in large tumors; however, the technique is more complicated and needs further evaluation [25].

In this study, few complications were encountered that were not life-threatening. We reported the occurrence of pain, low-grade fever, rise in the transaminases levels and one case of pleural effusion that resolved under conservative measures. In other series, the reported complications included creation of arteriovenous shunt due to needle puncture, burn due to inadequate grounding, biliary tree injury, peritonitis due to inadequate sterilization and seeding of tumor cells when track ablation maneuver was not applied [26].

The study included some lesions that were performed through open surgery such as lesions considered inaccessible through percutaneous technique or multiple lesions necessitating combination of surgical resection and RFA. Focal lesions at the dome of the liver were considered inaccessible by many authors and PEI was considered a better option; however, two patients in our series underwent a safe thoracoscopic approach that succeeded to obtain ablation without any recorded complications [27].

In conclusion, RFA is a highly effective technology for generating large volumes of necrotic tumor tissue. A variety of effective techniques exist to help reaching the maximum ablation results the aim of which is not fast ablation that may result in tissue charring but successful complete ablation of tumor mass.

REFERENCES

1. Lencioni R, Cioni D, Goletti O, Bartlozzi C. Radiofrequency thermal ablation of liver tumors: State-of-the-art. The Cancer J (review) 2000, 6: s304-s315.

2. Lai EC, Fan ST, Lo CM. Results of hepatic resection for hepatocellular carcinoma: an audit of 343 patients. Ann Surg 1995, 221: 291-298.

3. Kawasaki S, Makuuchi M, Miyagawa S. Results of hepatic resection for hepatocellular carcinoma. World J Surg 1995, 19: 31-34.

4. Bismuth H, Chiche L, Adam R. Liver resection versus transplantation for hepatocellular carcinoma in cirrhotic patients. Ann Surg 1993, 218: 145-151.

5. Hoffman AL, Wu SS, Obaid AK, French SW, Lois J, McMonigle M, Ramos HC, Sher LS, Lopez RR. Histologic evaluation and treatment outcome after sequential radiofrequency ablation and hepatic resection for primary and metastatic tumors. Am Surg 2002, 68 (12): 1038-43.

6. Chan RP, Asch M, Kachura J, Ho CS, Greig P, Langer B, Sherman M, Wong F, Feld R, Gallinger S. Radiofrequency ablation of malignant hepatic neoplasms. Can Assoc Radiol J 2002, 53 (5): 272-8.

7. Bowles BJ, Machi J, Limm WM, Severino R, Oishi AJ, Furumoto NL, Wong LL, Oishi RH. Safety and efficacy of radiofrequency thermal ablation in advanced liver tumors. Arch Surg 2001, 136 (8): 864-9.

8. Izzo F, Barnett CC Jr, Curley SA. Radiofrequency ablation of primary and metastatic malignant liver tumors. Adv Surg 2001, 35: 225-50.

9. Wood BJ, Ramkaransingh JR, Fojo T, Walther MM, Libutti SK. Percutaneous tumor ablation with radiofrequency. Cancer 2002, 94 (2): 443-51.

10. Owen RP, Ravikumar TS, Silver CE, Beitler J, Wadler S, Bello J. Radiofrequency ablation of head and neck tumors: dramatic results from application of a new technology. Head Neck 2002, 24 (8): 754-8.

11. Dupuy DE, Monchik JM, Decrea C, Pisharodi L. Radiofrequency ablation of regional recurrence from well-differentiated thyroid malignancy. Surgery 2001, 130 (6): 971-7.

12. Machi J, Uchida S, Sumida K, Limm WM, Hundahl SA, Oishi AJ, Furumoto NL, Oishi RH. Ultrasound-guided radiofrequency thermal ablation of liver tumors: percutaneous, laparoscopic, and open surgical approaches. J Gastrointest Surg 2001, 5 (5): 477-89.

13. Berber E Flesher N, Siperstein A. Initial clinical evaluation of the RITA 5- centimeter radiofrequency thrmal ablation catheter in the treatment of liver tumors. The Cancer J 2000, 6: s319-s329.

14. Iannitti DA, Dupuy DE, Mayo-Smith WW, Murphy B. Hepatic radiofrequency ablation. Arch Surg 2002, 137 (4): 422-6; discussion 427.

15. Curley SA, Izzo F. Radiofrequency ablation of hepatocellular carcinoma. Minerva Chir 2002, 57 (2): 165-76.

16. Curley SA, Izzo F. Radiofrequency ablation of primary and metastatic hepatic malignancies. Int J Clin Oncol 2002, 7 (2): 72-81.

17. Parikh AA, Curley SA, Fornage BD, Ellis LM. Radiofrequency ablation of hepatic metastases. Semin Oncol 2002, 29 (2): 168-82.

18. Kuvshinoff BW, Ota DM. Radiofrequency ablation of liver tumors: influence of technique and tumor size. Surgery 2002, 132 (4): 605-11.

19. Kosari K, Gomes M, Hunter D, Hess DJ, Greeno E, Sielaff TD. Local, intrahepatic, and systemic recurrence patterns after radiofrequency ablation of hepatic malignancies. J Gastrointest Surg 2002, 6 (2): 255-63.

20. Slakey DP. Radiofrequency ablation of recurrent cholangiocarcinoma. Am Surg 2002, 68 (4): 395-7.

21. Siperstein A, Gitomirski A. History and technological aspects of radiofrequency thermoablation. The Cancer J 2000, 6: s293-s303.

22. Shiina S, Teratani T, Obi S, Hamamura K, Koike Y, Omata M. Nonsurgical treatment of hepatocellular carcinoma: from percutaneous ethanol injection therapy and percutaneous microwave coagulation therapy to radiofrequency ablation. Oncology 2002, 62 Suppl 1: 64-8.

23. Barnett CC Jr, Curley SA. Ablative techniques for hepatocellular carcinoma. Semin Oncol 2001, 28 (5): 487-96.

24. Ikeda M, Okada S, Ueno H, Okusaka T, Kuriyama H. Radiofrequency ablation and percutaneous ethanol injection in patients with small hepatocellular carcinoma: a comparative study. Jpn J Clin Oncol 2001, 31 (7): 322-6.

25. Yamasaki T, Kurokawa F, Shirahashi H, Kusano N, Hironaka K, Okita K. Percutaneous radiofrequency ablation therapy for patients with hepatocellular carcinoma during occlusion of hepatic blood flow. Comparison with standard percutaneous radiofrequency ablation therapy. Cancer 2002, 95 (11): 2353-60.

26. Tamai F, Furuse J, Maru Y, Yoshino M. Intrahepatic pseudoaneurysm: a complication following radio-frequency ablation therapy for hepatocellular carcinoma. Eur J Radiol 2002, 44 (1): 40-3.

27. Kurokohchi K, Watanabe S, Masaki T, Hosomi N, Funaki T, Arima K, Yoshida S, Miyauchi Y, Kuriyama S. Combined use of percutaneous ethanol injection and radiofrequency ablation for the effective treatment of hepatocelluar carcinoma. Int J Oncol 2002, 21 (4): 841-6.