HPB, 2007; 9: 363-367

informa

healthcare

ORIGINAL ARTICLE

Evaluation of mulitprobe radiofrequency technology in a porcine model

WILLIAM W. HOPE[1], JASON M. ARRU[1], JASON Q. MCKEE[2], DENNIS VROCHIDES[2],
BASSAM ASWAD[2], CAROLINE J. SIMON[2], DAMIAN E. DUPUY[2] & DAVID A. IANNITTI[1]

[1] *Division of Gastrointestinal and Minimally Invasive Surgery. Carolinas Medical Center, Charlotte, NC, and* [2]*Department of Surgery and Diagnostic Imaging, Brown Medical School, Providence, RI, USA*

Abstract

Objective. We evaluated two new radiofrequency devices in an *in vivo* porcine model. *Materials and methods.* Multiprobe radiofrequency ablation (RFA) was used in a porcine model with an impedance-based algorithm in one experiment and clustered probes with and without switcher controllers in another; a Pringle maneuver was used with half of the ablations. *Results.* The impedance experiment included 13 ablations, with a mean length of 7.0 cm and width of 2.9 cm (95% CI) and an average time of 596 s. Ablation volumes were significantly larger (54.1 ± 11.7 cc^3 vs 34.9 ± 4.8 cc^3, $p<0.05$) and ablation times were significantly shorter (359 s vs 834 s, $\rho <0.05$) for the Pringle group compared with the No Pringle group, respectively. The switcher controller experiment included 34 RFAs. Diameter (mm) (51.4 vs 40.3, $p <0.0001$), surface area (cm^2) (22.4 vs 16.0, $\rho <0.0002$), and volume (cc) (66.1 vs 36.9, $\rho <0.0001$) were significantly larger for the combination probes with switcher controller compared with clustered probes, respectively. Ablation volumes for the Pringle vs No Pringle groups in the combination probes were 68.0 cc vs 64.3 cc and for the clustered probes 40.1 cc vs. 33.7 cc, respectively. *Conclusion.* Multiprobe ablations using RFA are promising technologies that need further study to evaluate their clinical utility.

Key Words: *Ablation, multiprobe, radiofrequency ablation, liver*

Introduction

Ablation techniques are becoming an important treatment option for unresectable malignant liver tumors. With the increase in minimally invasive surgery, many ablative techniques for treatment of liver tumors have been developed including ethanol injection and thermal ablation techniques such as radiofrequency, laser, microwave, high frequency ultrasound, and cryotherapy. The benefits of these techniques are low morbidity and the flexibility of treatment.

Radiofrequency ablation (RFA) is the most widely accepted of the thermal ablative techniques for liver tumors and shows good efficacy, with the ability to obtain good local control of tumors and minimal complications [1]. One shortcoming of current ablative technology is the small size of coagulation zones, which limits its use in large tumors. The purpose of our study was to evaluate new technology associated with radiofrequency and determine if larger coagulation zones can be produced.

Materials and methods

Experimental protocols were approved by the Brown University Institutional Review Board and the Institutional Animal Care and Use Committee satisfying the guidelines of the US Public Health Service.

In the first experiment, two monopolar 3.0 cm LeVeen® (Boston Scientific, Natick, MA, USA) RFA probes spaced 3.5 cm apart were deployed in an *in vivo* porcine liver. The pigs used in this experiment had an average weight of 56 kg (range 31-101 kg). Ablations were accomplished with a 200 W radiofrequency generator according to an impedance-based algorithm with a Pringle maneuver used with half of the ablations. The liver was then removed for gross and histologic assessment. The main outcome

Data from this original research were presented as a poster at the annual meeting of the Society of Surgical Oncology, Washington, DC, March 15-18, 2007.

Correspondence: David A. Iannitti, MD, FACS, Chief, Hepatopancreaticobiliary Surgery, Division of Gastrointestinal and Minimally Invasive Surgery, Department of Surgery, Carolinas Medical Center, 1000 Blythe Blvd, MEB 601, Charlotte, NC 28203, USA. Tel: +1 704 355 6220. Fax: +1 704 355 4822. E-mail: David.Iannitti@carolmashealthcare.org

(Received 18 June 2007; accepted 4 August 2007)

ISSN 1365-182X print/ISSN 1477-2574 online
DOI: 10.1080/13651820701611218

measures were ablation dimensions, time to roll-off, and histologic evaluation. Roll-off is defined as a rapid increase in impedance. The treatment algorithm included two phases and is shown in Table I. Phase I began with 80 W and increased by 20 W every minute until roll-off. Phase II began at 120 W and increased by 20 W every minute until roll-off.

In the second experiment, multiprobe RFAs were performed in 12 porcine livers using a 200 W radiofrequency generator. Pigs ranged in weight from 40 to 80 kg. A Pringle maneuver was used with half of the ablations. Times of ablations were documented for the combination probes with switcher controller and standard clustered probes. Three 3.0 cm active tip Cooled-Tip™ single probes (Valleylab™, Boulder, CO, USA) spaced 2.0 cm apart with switcher controller were compared with standard clustered Cooled-Tip radiofrequency probes. The switcher controller was set to a maximum of 30 ohms above baseline for 30 s. The liver was then removed for gross and histologic assessment.

The goal of ablation is to apply current to surrounding tissues. The ability to apply current is directly related to tissue impedance. As tissue impedance increases, the amount of current that can be applied decreases. When multiple probes are used, the goal is to transfer current from one electrode to the next to limit the amount of impedance. This in turn limits the amount of tissue desiccation and allows more current to be applied to the tissue. The function of the switcher controller is to actively transfer current from one electrode to the next to try and prevent tissue desiccation and increased impedance. In this experiment, the switcher controller was set to a max of 30 s or 30 ohms, meaning that the current would switch to the next electrode after 30 s or when the impedance reached 30 ohms, whichever came first.

For all experiments, pigs underwent general inhaled anesthesia with maintenance intravenous fluids of lactated Ringer's solution. Routine monitoring including blood pressure, pulse, oxygen saturations, and temperature was performed during all procedures. Approximately one to three ablations were performed in each pig. Probe placement was determined using ultrasound guidance, trying to avoid proximity to major blood vessels. Ablations were started peripherally and then moved centrally to try and avoid hypoperfusion of the liver during ablations. Zones of ablations were measured grossly using a caliper. Livers were sectioned perpendicular to the zone of the ablation to measure the maximum ablation diameter.

Table I. Impedance-based treatment algorithm (porcine).

Time (min)	Power (W)	Impedance (ohms)
	Phase I	
0:15	84	48
1:15	102	40
2:15	118	41
3:15	141	41
4:15	162	41
5:15	181	47
6:21	Roll-off	
	Phase II	
0:15	125	42
1:15	133	54
2:41	Roll-off	

For all experiments, descriptive statistics including means and standard deviations or counts and percentages were calculated. The Student's t test was used to compare means between the two groups. SAS® software version 9.1 (SAS Institute, Cary, NC, USA) was used for all analyses. A p value of < 0.05 was considered statistically significant.

Results

For the impedance experiment, 13 ablations were undertaken in 8 pigs. One ablation was excluded due to no roll-off. Ablation characteristics included a mean length of 7.0 cm and width of 2.9 cm (95% CI; length, range 6.9-7.1 cm; width, range 1.8-4.0 cm) with an average time of 596 s. Ablation volumes were significantly larger (54.1 ± 11.7 cc^3 vs 34.9 ± 4.8 cc^3 , $\rho < 0.05$) and ablation times were significantly less (359 s vs 834 s, $p < 0.05$) for the Pringle group compared with the No Pringle group, respectively. Ablation shape was also different between the two groups. In the No Pringle group, the ablation was dumbbell-shaped with circular ablations produced by each electrode with a small connection in between. In the Pringle group, the ablation shape was more oval with increase in the ablation size between the two electrodes. Ablation characteristics are listed in Table II.

The second experiment consisted of 34 total RFAs in porcine livers. Ablations for the combination probes with switcher controller were 8 min for the Pringle group and 16 min for the No Pringle group. Ablation times for the clustered probes were 6 min for the Pringle group and 12 min for the No Pringle group. Ablation characteristics are shown in Tables III and IV. Diameter (51.4 mm vs 40.3 mm, $\rho < 0.0001$), surface area (22.4 cm^2 vs 16.0 cm^2, $\rho < 0.0002$), and volume (66.1 cc vs 36.9 cc, $p < 0.0001$) were significantly larger for the combination probes with switcher controller compared with the standard clustered probes, respectively. There were no differences in ablation shape for the Pringle and No Pringle group for this experiment. Ablation volumes for the Pringle vs No Pringle groups in the combination probes were 68.0 cc vs 64.3 cc and for the clustered probes 40.1 cc vs 33.7 cc, respectively.

Table II. Ablation characteristics for impedance-based radiofrequency ablation (porcine).

Parameter	Pringle maneuver (n = 6)	No Pringle maneuver (n = 6)	*ρ* value
Ablation times (s)	359	834	<0.05
Ablation length (cm)	6.9	7.0	NS
Ablation width - lateral (cm)	3.4	2.9	NS
Ablation width - central (cm)	3.1	2.1	NS
Ablation volumes (cc^3)	54.1 ± 11.7	34.9 ± 4.8	<0.05

Table III. Ablation characteristics for combination probes with switcher controller and clustered radiofrequency probes (porcine).

Probes	Diameter (mm)	Surface area (cm^2)	Volume (cc)
Cluster	40.3±4.3	16.0±3.3	36.9±9.5
Combination	51.4±7.4	22.4±4.7	66.1±17.9
ρ value	< 0.0001	0.0002	< 0.0001

Discussion

Malignant hepatic tumors are a challenging problem for all clinicians. The American Cancer Society estimates that 18 510 new cases of primary liver and intrahepatic bile duct tumors and 148 610 cases of colorectal cancer were diagnosed in the USA in 2006 [2]. Of the patients with colorectal cancer in 2006, 25% have metastatic disease [2]. Few cases of liver cancer are diagnosed in the early stages of disease due to the lack of signs and symptoms. Therefore, few patients are candidates for surgical removal, with <30% who undergo exploratory surgery for liver cancer able to undergo surgical resection [2]. In addition, only 10-20% of patients with colorectal carcinoma metastases are candidates for liver resection [2].

Because a majority of hepatic tumors are unresectable at the time of diagnosis, there is much interest in local thermal ablative technologies. RFA is the most widely adopted thermal ablative technology and is reported to be safe and efficacious [3-5]. RFA destroys tumors by increasing tissue temperature, which causes coagulative necrosis [6]. Alternating high frequency current displaces molecules in one direction and then the other [7]. The molecules in the tissue surrounding the probe follow the changes in the current, which causes friction between molecules and produces heat. The heat is focused near the electrode due to the size difference between the small surface area of the electrode and the large area of the grounding pad [8]. Temperatures >55°C are linked to tissue necrosis [9]. The RFA systems apply heat of approximately 90°C. Increasing the temperature to >110°C causes tissue desiccation and decreases the efficacy of RFA due to current impedance [10].

One common criticism of RFA and local thermal ablations in general is the difficulty in treating large tumors, defined as > 3 cm in diameter [11]. Treatment of large tumors can be time-consuming, because they require sequential overlapping ablations to ensure adequate coverage [12,13]. New technologies use several probe needles rather than a single probe and use cooler electrodes. By using several probes, a greater surface area can be effectively treated. Probe cooling is done by using a dual lumen probe with constant flow of cooled liquid to decrease the temperature at the electrode-tissue interface. This increases the time for application and results in increased energy delivery [7]. Goldberg and colleagues evaluated the impact of using multiprobe RFA arrays and found that probes spaced 1.5 cm or less apart acted synergistically, producing a larger total volume of coagulated tissue than single RFA probes [14].

In our study, we evaluated the use of multiprobe ablation using RFA technology. We demonstrated that, in impedance-based RFA, two probes had a synergistic effect, which resulted in ablation areas larger than the areas for individual burns. We also found that the

Table IV. Ablation characteristics for combination probes with switcher controller and clustered radiofrequency probes with and without application of the Pringle maneuver (porcine).

Probes	Diameter (mm)		Surface area (cm^2)		Volume (cc)	
Cluster	40.3±4.3		16.0±3.3		36.9 ±9.5	
	Pringle maneuver	No Pringle maneuver	Pringle maneuver	No Pringle maneuver	Pringle maneuver	No Pringle maneuver
	42.5	38.1	17.6	14.2	40.1	33.7
Combination	51.4±7.4		22.4 ±4.7		66.1 ±17.9	
	Pringle maneuver	No Pringle maneuver	Pringle maneuver	No Pringle maneuver	Pringle maneuver	No Pringle maneuver
	54.5	48.2	23.9	20.8	68.0	64.3

Table V. Overall average ablation volumes for multiprobe radiofrequency and microwave technology.

Parameter	RFA cluster porcine	Bipolar impedance (porcine)	Multiprobe output (porcine)	Microwave cluster (human)
Average ablation volume (cm^3)	36.9	44.5	66.1	50.8*

*From Simon et al. [15].

volume of thermocoagulation was significantly larger and the central area of ablation was more consistent in the Pringle group with significantly less ablation time. While this finding was not unexpected due to the known heat-sink effect that blood vessels have on RFA, it is important to note this using bipolar impedance probes, which are now available.

We also demonstrated that the use of the switcher controller with combination probes consistently facilitated larger ablation diameter, surface area, and volumes compared with a standard clustered probe, and the use of the Pringle maneuver resulted in similar size ablations in half the time.

Future research in the field of ablation needs to focus on the limitations of obtaining larger ablation zones. Basic science projects currently include the evaluation of ablation methods that may create larger ablation volumes, including ablation-enhancing solutions. Algorithms for optimal power and current to be applied to tissue also require further study. Perhaps by not heating tissue at a rapid rate, we can avoid tissue desiccation, prevent impedance, and allow increasing current to reach the tissue. Other areas of active research include alternative methods of ablation, including microwave ablation (MWA), electroporation, and laser therapy.

Microwave ablation is a thermal ablation technique that uses electromagnetic energy to cause coagulation necrosis. While RFA and MWA share many similarities, they differ substantially in the basic mechanism of energy deposition. RFA uses the flow of current through conducting electrodes within body tissue, and MWA uses an electromagnetic field around an insulated and electrically independent antenna. Because of this, MWA is theoretically more amenable to the simultaneous use of multiple antennae to achieve larger coagulation volumes.

Recently, MWA was evaluated in an ablate and resect trial in liver tumors using a 915 MHz microwave ablation system [15]. They reported an average ablation zone of 50.8 cm^3 using a setting of 45 W for 10 min in 10 patients who were scheduled to undergo liver resection [15]. Clinical studies have also showed efficacy for microwave ablation in unresectable liver tumors [16]. When evaluating the various multiprobe modalities used in this study and from the recent microwave study, clustered probes with switcher controller had the highest ablation volume, followed by microwave, bipolar impedance-based RFA, and finally clustered RFA without switcher controller, with average ablation volume ranging from 36.9 cm to 66.1 cm^3 (Table V).

In conclusion, multiprobe ablation for impedance- and output-based systems facilitates larger ablation volumes. Both RFA probes produced similar ablations in half of the time when using the Pringle maneuver. Further studies are needed to evaluate multiprobe RFA ablation and their role in the treatment of large liver tumors.

Acknowledgements and disclosures

Research support: Boston Scientific, Valleylab™

References

[I] Chen MH, Yang W, Yan K, Gao W, Dai Y, Wang YB, et al. Treatment efficacy of radiofrequency ablation of 338 patients with hepatic malignant tumor and the relevant complications. World J Gastroenterol 2005; 11:6395-401.

[2] American Cancer Society. Cancer facts and figures. Atlanta, GA: American Cancer Society, 2006.

[3] Lau WY, Leung TW, Yu SC, Ho SK. Percutaneous local ablative therapy for hepatocellular carcinoma: a review and look into the future. Ann Surg 2003;237:171-9.

[4] Curley SA. Radiofrequency ablation of malignant liver tumors. Ann Surg Oncol 2003;10:338-47.

[5] Scaife CL, Curley SA. Complication, local recurrence, and survival rates after radiofrequency ablation for hepatic malignancies. Surg Oncol Clin N Am 2003;12:243-55.

[6] McGahan JP, Brock JM, Tesluk H, Gu WZ, Schneider P, Browning PD. Hepatic ablation with use of radio-frequency electrocautery in the animal model. J Vasc Interv Radiol 1992; 3:291-7.

[7] Siperstein A, Gitormirskj A. History and technological aspects of radiofrequency thermal ablation. Cancer J 2000;6: 5293-303.

[8] 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.

[9] Rossi S, Fornari F, Pathies C, Buscarini L. Thermal lesions induced by 480 KHz localized current field in guinea pig and pig liver. Tumori 1990;76:54-7.

[10] Decadt B, Siriwardena AK. Radiofrequency ablation of liver tumours: systematic review. Lancet Oncol 2004;5:550-60.

[II] Livraghi T, Goldberg SN, Lazzaroni S, Meloni F, Ierace T, Solbiati L, et al. Hepatocellular carcinoma: radio-frequency ablation of medium and large lesions. Radiology 2000;214: 761-8.

[12] Dodd GD 3rd, Frank MS, Aribandi M, Chopra S, Chintapalli KN. Radiofrequency thermal ablation: computer analysis of the size of the thermal injury created by overlapping ablations. AJR Am J Roentgenol 2001;177:777-82.

[13] Chen MH, Yang W, Yan K, Zou MW, Solbiati L, Liu JB, et al. Large liver tumors: protocol for radiofrequency ablation and its clinical application in 110 patients - mathematic model, overlapping mode, and electrode placement process. Radiology 2004;232:260-71.

[14] Goldberg SN, Gazelle GS, Dawson SL, Rittman WJ, Mueller PR, Rosenthal DI. Tissue ablation with radiofrequency using multiprobe arrays. Acad Radiol 1995;2:670-4.

[15] Simon CJ, Dupuy DE, Iannitti DA, Lu DS, Yu NC, Aswad BI, et al. Intraoperative triple antenna hepatic microwave ablation. AJR Am J Roentgenol 2006;187:W333-40.

[16] Iannitti DA, Martin RC, Simon CJ, Hope WW, Newcomb WL, McMasters KM, et al. Hepatic tumor ablation with clustered microwave antennae: the US Phase Π Trial. HPB 2007;9:120-4.