Radiat Med (2008) 26:408–414
DOI 10.1007/s11604-008-0251-x

ORIGINAL ARTICLE

Simultaneous microwave ablation using multiple antennas in explanted bovine livers: relationship between ablative zone and antenna

Fumiyoshi Oshima · Koichiro Yamakado
Atsuhiro Nakatsuka · Haruyuki Takaki
Masashi Makita · Kan Takeda

Received: February 6, 2008 / Accepted: April 11, 2008

Abstract
Purpose. Our purpose was to determine the optimal antenna spacing to achieve large ablative zones without indentations when microwave ablation is performed with simultaneous activation of two or three antennas.
Materials and methods. Microwave ablation was performed with single-antenna activation and simultaneous activation of two or three antennas with a spacing of 1.5, 2.0, 2.5, or 3.0 cm in explanted bovine livers. Microwave energy was applied for 10 min with a power of 45 W. The shapes and sizes of the ablative zones created were recorded and compared. *Results.* The shape of the ablative zone was ellipsoid in the axial plane (along the antenna axis) and spherical in the transverse plane (perpendicular to the antenna axis) in single-antenna ablation. The ablative zones were spherical or ellipsoid in both the axial and transverse planes in two- and three-antenna ablation with an antenna spacing of 2.0 cm or less. Indentations were observed between the ablative zones created by the antennas when the spacing was 2.5 cm or more, reducing the minimum transverse diameter. When two- or three-antenna ablation was performed with a spacing of 2.0 cm or less, the axial and minimum transverse diameters were significantly larger than in single-antenna ablation. The largest volume (almost two or three times the single-activation volume) was achieved in two- or three-antenna ablation with an antenna spacing of 2.0 cm.
Conclusion. We found that simultaneous microwave ablation using multiple microwave antennas creates large ablative zones without indentations when multiple antennas are activated with an antenna spacing of 2.0 cm or less.

Key words Microwave · Multiple antennas · Simultaneous · Cancer · Synergetic effect

Introduction

Recently, minimally invasive techniques such as radiofrequency (RF) ablation and microwave ablation have been used for the treatment of unresectable liver neoplasms under imaging guidance.[1–13] However, microwave ablation is less commonly employed than RF ablation in clinical practice, because a larger number of treatment sessions are needed to treat even small tumors.[11–13] One advantage of microwave ablation is that it is theoretically more amenable to the simultaneous activation of multiple antennas to obtain larger ablative zones.[9,10,14–17] The heat produced by microwave energy, in contrast to that produced by RF energy, is not dependent on the passage of an electrical current through the tissues, allowing the simultaneous activation of multiple antennas without electrical interference.[15–17]

It is important to determine the expected size and shape of a single-session ablative zone and its relationship to the microwave antenna used to achieve complete tumor ablation in fewer treatment sessions. A number of studies have already reported the usefulness of simultaneous activation of multiple antennas for obtaining large ablative zones in clinical and in vivo studies.[9,10,14–17] However, there are few ex vivo data concerning the size

F. Oshima · K. Yamakado (✉) · A. Nakatsuka · H. Takaki · M. Makita · K. Takeda
Department of Radiology, Mie University School of Medicine, 2-174 Edobashi, Tsu 514-8507, Japan
Tel. +81-59-231-5029; Fax +81-59-232-8066
e-mail: yama@clin.medic.mie-u.ac.jp

Table 1. Ablative zone size and shape in the transverse plane and ellipticity index

Number of antennas	Antenna spacing (cm)	Mean AD (cm)	Mean TD_{max} (cm)	Mean TD_{min} (cm)	Volume (cm^3)	Shape in axial plane	Shape in transverse plane	Ellipticity index
One		4.1 ± 0.2	2.7 ± 0.1	2.5 ± 0.2	14.1 ± 1.6	Elliptical	Spherical	1.6 ± 0.1
Two	1.5	4.7 ± 0.1*†	3.7 ± 0.1	3.0 ± 0.4*†	27.1 ± 3.4*	Elliptical	Spherical	1.4 ± 0.1
	2.0	4.7 ± 0.1*†	4.4 ± 0.5	3.0 ± 0.1*†	31.6 ± 4.9*‡	Elliptical	Elliptical	1.3 ± 0.1
	2.5	4.2 ± 0.2	4.5 ± 0.1	2.3 ± 0.2	24.2 ± 3.4*	Butterfly	Butterfly	—
	3.0	4.2 ± 0.2	4.8 ± 0.1	1.9 ± 0.4	26.3 ± 5.3*	Butterfly	Butterfly	—
Three	1.5	5.6 ± 0.2*†	4.2 ± 0.4	3.5 ± 0.2*	43.5 ± 6.3*†	Elliptical	Spherical	1.5 ± 0.1
	2.0	4.9 ± 0.2*†	4.5 ± 0.2	4.2 ± 0.2*‡	47.5 ± 6.2*†‡	Elliptical	Spherical	1.1 ± 0.1
	2.5	4.4 ± 0.2	4.9 ± 0.3	3.4 ± 0.2*	38.7 ± 4.2*	Butterfly	Butterfly	—
	3.0	4.3 ± 0.2	5.0 ± 0.3	3.0 ± 0.5	33.2 ± 2.1*	Butterfly	Butterfly	—

AD, axial diameter; TD, transverse diameter
* $P < 0.01$ vs. single antenna; † $P < 0.01$ vs. spacing of 2.5 cm and 3 cm in the same group; ‡ $P < 0.05$ vs. than any other spacing in the same group

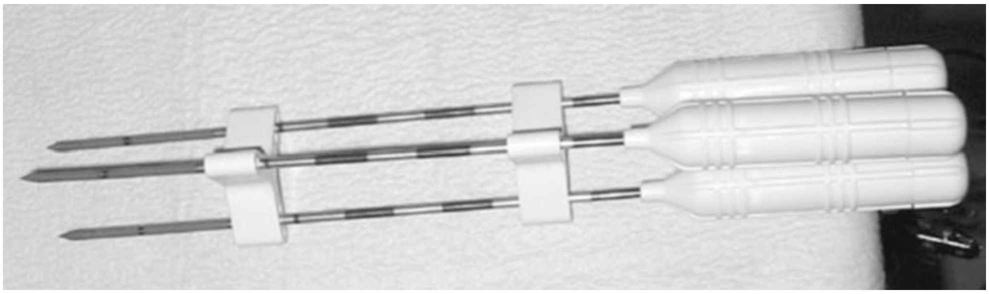

Fig. 1. Two or three microwave antennas were placed in the liver parallel to each other using two spacers. Three antennas were placed in a triangular configuration

and geometry of single-session ablative zones created by the simultaneous activation of multiple antennas. In particular, it is important to determine the optimal antenna spacing for maximizing the size of the ablative zone without indentations between the ablative zones created by the antennas, as the presence of such indentations makes it difficult to estimate the ablative zone size.

In the present study, the optimal antenna spacing to achieve large ablative zones without indentations when two or three microwave antennas are activated simultaneously was investigated by performing ablation with various antenna spacings in explanted bovine livers.

Materials and methods

Ex vivo bovine liver microwave ablation

Microwave ablation was performed in explanted bovine livers with a mean weight of 5.9 kg (4.7–6.4 kg) using a microwave ablation system (Vivant Medical, Mountain View, CA, USA). Single-session microwave ablation was performed with single-antenna activation and with simultaneous two- or three-antenna activation. Multiple antennas were simultaneously activated with an antenna spacing of 1.5, 2.0, 2.5, or 3.0 cm. Thus, microwave ablation was performed under nine sets of conditions based on the number of antennas and the antenna spacing (Table 1). Seven ablative zones were created under each set of conditions, for a total of 63 ablative zones.

Straight 13G antennas with a length of 15 cm and a 3.6-cm radiating tip were employed (Viva Tip; Vivant Medical). The antennas were placed into explanted bovine livers to a depth of 7 cm. When two or three antennas were placed, two spacers were used to ensure that the antennas were parallel to each other (Fig. 1). Three antennas were placed in a triangular configuration. After the antennas were placed in the liver, each antenna was connected to a separate microwave generator (Viva Wave, Vivant Medical). For two-antenna ablation, two generators were used, and for three-antenna ablation, three generators were used. Each generator was capable of generating 60 W power at 915 MHz. Microwave ablation was performed at 45 W for 10 min.

Assessment

Descriptions of the shapes and sizes of the ablative zones were based on the two sets of guidelines proposed by Mulier et al.[18] and by Goldberg et al.[19] The axial plane was defined as the plane along the antenna axis (Figs. 2a, 3a, 4a), and the transverse plane was defined as the plane perpendicular to the axial plane. The liver specimens were first cut along the antenna axis (axial

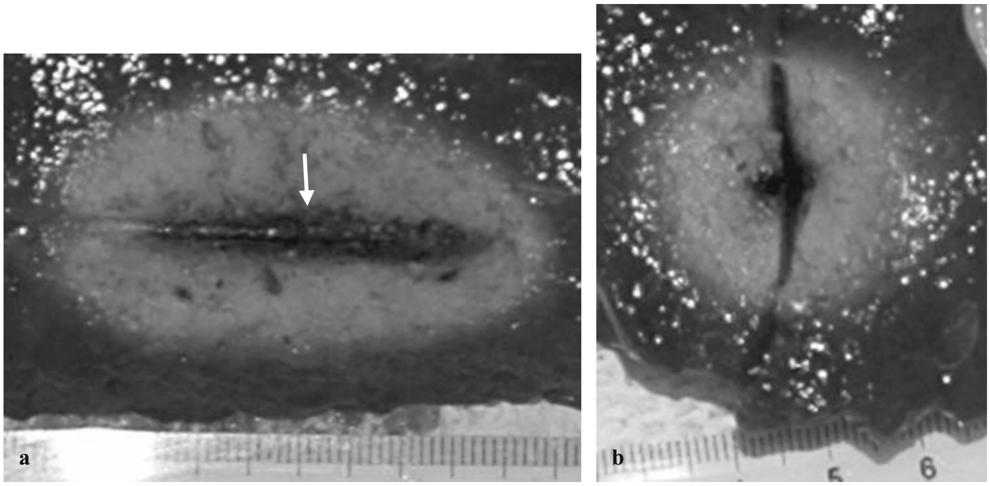

Fig. 2. Photographs of an ablative zone created by microwave ablation using a single microwave antenna. **a** Axial plane along the antenna axis (*arrow*). The ablative zone shape is ellipsoid. The mean axial diameter is 4.1 ± 0.2 cm. **b** Transverse plane perpendicular to the axial plane. The ablative zone shape is spherical, with mean maximum and minimum transverse diameters of 2.7 ± 0.1 cm and 2.5 ± 0.2 cm, respectively

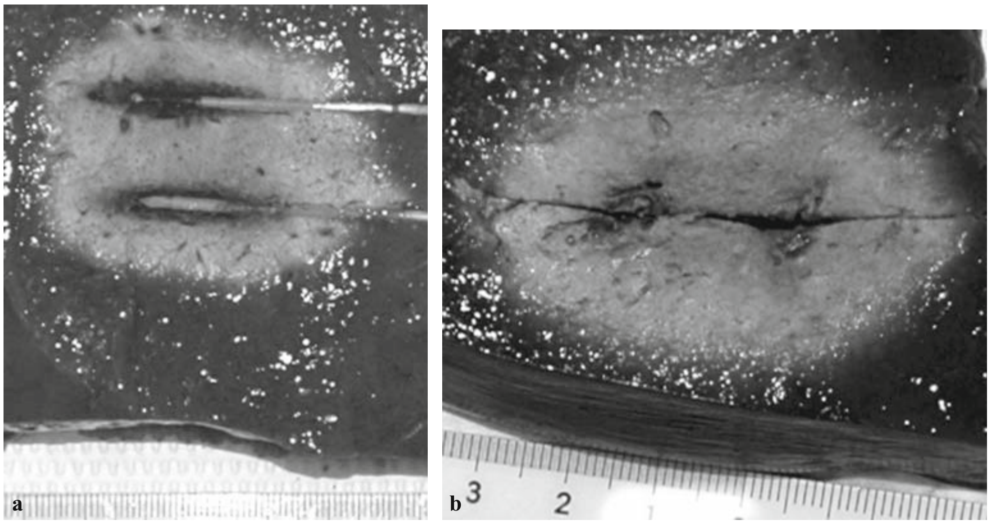

Fig. 3. Photographs of an ablative zone created by simultaneous two-antenna activation with a spacing of 2.0 cm. **a** The ablative zone shape in the axial plane is ellipsoid, with no indentations observed between the ablative zones created by the two antennas. The mean axial diameter is significantly larger than that in single-antenna activation (4.7 ± 0.1 cm). **b** The ablative zone shape in the transverse plane is ellipsoid, with no indentations observed between the ablative zones created by the two antennas. The maximum transverse diameter increases as the antenna spacing is increased (see Fig. 4b). The mean minimum diameter in the transverse plane is significantly larger than that in single-antenna ablation (3.0 ± 0.1 cm)

plane) and then cut perpendicular to the axial plane (transverse plane) with a slice thickness of 5 mm. The ablative zone size was measured in the section showing the largest transverse diameter.

Shape descriptions and size measurements of the ablative zones were the responsibility of two of the authors (F.O., M.M.), with the final results based on consensus.

The shapes in both the axial and transverse planes were evaluated visually. Descriptions of ablative zone size were based on whether they were spherical, ellipsoid, or butterfly shaped. A spherical or ellipsoid shape indicates complete fusion of the ablative zones created by the respective antennas, whereas a butterfly shape indicates incomplete fusion of the ablative zones created by the respective antennas, resulting in indentations between the ablative zones.

The axial diameter (AD) is defined as the maximum distance in centimeters (cm) between the proximal and distal edges of the ablative zone in the axial plane. The maximum transverse diameter (TD_{max}) is defined as the maximum distance in centimeters between two opposite edges of the ablative zone in the transverse plane. The minimum transverse diameter (TD_{min}) is defined as the minimum distance in centimeters between two opposite edges of the ablative zone in the transverse plane,

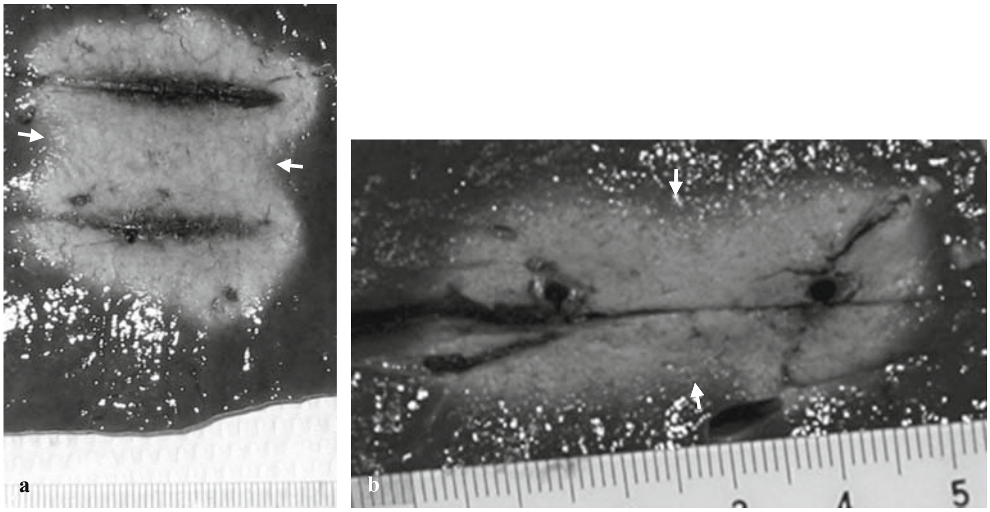

Fig. 4. Photographs of an ablative zone created by simultaneous two-antenna activation with a spacing of 2.5 cm. **a** In the axial plane, indentations (*arrows*) are clearly observed between the ablative zones created by the two antennas. No significant increase is noted in the mean axial diameter as compared with single-antenna ablation (4.2 ± 0.2 cm). **b** In the transverse plane, the ablative zone shows a butterfly shape, and indentations (*arrows*) are seen between the ablative zones created by the two antennas. No significant difference is noted in the mean minimum transverse diameter as compared with single-antenna ablation (2.3 ± 0.2 cm)

measured along a line crossing the midpoint of the line of the maximum transverse diameter. The shapes of the ablative zones in the transverse plane were recorded.

When the ablative zone was spherical or ellipsoid, the approximate volume of the ablative zone was calculated using the following formula:

$$\text{Volume} = \pi/6 \times TD_{min} \times TD_{max} \times AD\ (MAD)$$

When indentations were observed in the ablative zone, the ablative zone volume was calculated by multiplying the area in each slice by the slice thickness of 5 mm. For spherical and ellipsoid ablative zones, the ellipticity index (EI) was calculated. The EI value quantitatively describes the overall shape of the ablative zone in the axial plane and is calculated as the ratio of the axial diameter or midaxial diameter to the mean transverse diameter:

$$EI = 2AD/(TD_{max} + TD_{min})$$

An EI value of 1.0 roughly corresponds to a spherical ablative zone, a value greater than 1.0 to an ellipsoid ablative zone, and a value less than 1.0 to a flattened spherical ablative zone.[18] An EI value close to 1.0 therefore indicates a more even spread.

Statistical analysis

Results are presented as mean ± standard deviation. Ablative zone sizes were compared using the Wilcoxon rank-sum test. A P value less than 0.05 was considered to be statistically significant.

Results

Ablative zone shape

The ablative zone shapes in the axial and transverse planes and the EI values are summarized in Table 1. The ablative zone shape was ellipsoid in the axial plane and spherical in the transverse plane in single-antenna ablation (see Fig. 2a,b). Both the axial and transverse planes were ellipsoid or spherical in two- or three-antenna ablation when ablation was performed with an antenna spacing of 1.5 or 2.0 cm (Figs. 2a,b, 5), and no indentations were observed between the ablative zones created by the respective antennas. However, when two- or three-antenna ablation was performed with an antenna spacing of 2.5 cm or more, indentations appeared between the ablative zones created by the respective antennas, and the ablative zones appeared butterfly shaped in both the axial and transverse planes (Figs. 4a,b, 6a,b).

The EI value of the ablative zones was 1.6 ± 0.1 in single-antenna ablation. The EI value tended to approach 1.0 when two or three antennas were simultaneously activated with an antenna spacing of 2.0 cm (1.3 ± 0.1 for two antennas and 1.1 ± 0.1 for three antennas).

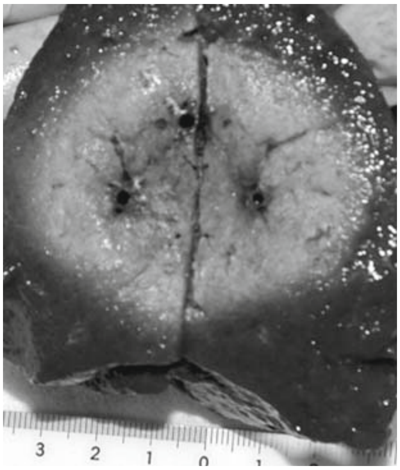

Fig. 5. Photograph in a transverse plane of an ablative zone created by simultaneous three-antenna activation with a spacing of 2.0 cm. The ablative zone shape is nearly spherical. The mean minimum transverse diameter (4.2 ± 0.2 cm) is larger than that obtained with any other antenna spacing and is close to the mean axial diameter (4.9 ± 0.2 cm) and the maximum diameter (4.5 ± 0.2 cm)

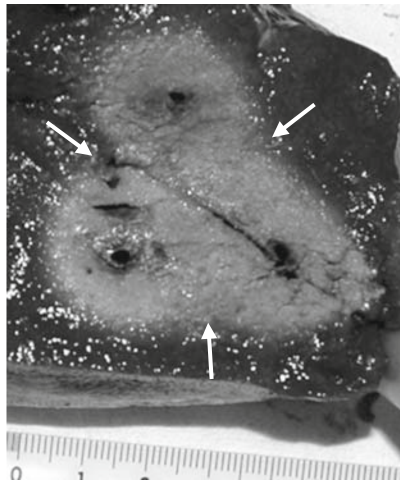

Fig. 6. Photograph in a transverse plane of an ablative zone created by simultaneous three-antenna activation with a spacing of 2.5 cm. Indentations are observed between the ablative zones created by the three antennas (*arrows*). Although the mean maximum transverse diameter (4.9 ± 0.3 cm) increases as the antenna spacing is increased, the mean axial diameter (4.4 ± 0.2 cm) and minimum transverse diameter (3.4 ± 0.2 cm) are significantly reduced as compared with three-antenna activation with a 2-cm spacing

Ablative zone size

The results of ablative zone size measurements are summarized in Table 1. The mean axial diameter was 4.1 ± 0.2 cm in single-antenna ablation (Fig. 2a). The axial diameter was significantly increased in two- or three-antenna ablation, as compared with single-antenna ablation, when the antenna spacing was 2.0 cm or less (Fig. 3a), but a significant increase was not observed when the antenna spacing was 2.5 cm or more (Fig. 4a).

The mean maximum transverse diameter was 2.7 ± 0.1 cm in single-antenna ablation (see Fig. 2b). The diameter increased as the antenna spacing was increased in two- or three-antenna ablation (see Figs. 3b, 4b, 5, 6).

The mean minimum transverse diameter was 2.5 ± 0.2 cm in single-antenna ablation (Fig. 2b). The minimum diameter showed a significant increase, as compared with single-antenna ablation, when two- or three-antenna ablation was performed with an antenna spacing of 2.0 cm or less (see Figs. 3b, 5). However, a significant increase was not observed when the antenna spacing was 2.5 cm or more, because the indentations between the ablative zones created by the respective antennas resulted in a smaller minimum transverse diameter (see Figs. 4b, 6).

The ablative zone volume obtained by single-antenna activation was 14.1 ± 1.6 cm^3. The volumes obtained by two- or three-antenna activation were significantly larger than the single-activation volume regardless of the antenna spacing. In both two- and three-antenna ablation, the volume was largest when the antenna spacing was 2.0 cm.

Discussion

The results of the present study show that microwave ablation with the simultaneous activation of two or three antennas is useful for creating ablative zones that are larger than those obtained by single-antenna ablation in the same ablation time. In the clinical setting, it is possible to place multiple antennas based on the shape of the tumor and to ablate the tumor "from the outside in."[9] However, indentations are observed between the ablative zones created by each antenna when ablation is performed with an antenna spacing of 2.5 cm or more. The presence of such indentations makes it difficult to determine whether the ablative zone encompasses the entire tumor. Based on the results of this study, it is recommended that the antenna spacing should be 2.0 cm or less to avoid indentations and obtain a larger ablative zone. Given the radius of the transverse diameter of the ablative zone created by single-antenna activation (1.25–1.35 cm), indentations should be observed between the ablative zones created by two antennas separated by 2.0 cm. We speculate that a synergetic effect occurs when the antenna spacing is 2.0 cm or less. The ablative zone volumes created by two- and three-antenna activation with an antenna spacing of 2.0 cm were almost two times and three times the single-antenna volume, respectively. Considering the overlapping volume, this phenomenon appears to be well explained by a synergetic effect resulting from the simultaneous activation of multiple antennas.

A number of in vivo experimental and clinical studies have shown results similar to those of the present study with regard to the relationship between indentations and the antenna spacing. Wright et al.[15] performed microwave ablation with simultaneous three-antenna activation in porcine livers and reported that a microwave antenna spacing of 1.7 cm or less yielded significantly more confluent and rounder lesions. However, when the antenna spacing was greater than 1.7 cm, clefts began to appear and the lesion shapes become less round. In the human liver, Simon et al.[14] and Yu et al.[9] treated liver tumors by activating three microwave antennas with an antenna spacing of 1.5–2.5 cm. Although a loss of border convexity was noted in some cases, concave clefts were not observed.

In terms of ablative zone size, the results of the present study are similar to those reported in previous in vivo and clinical studies.[9,14–16] This finding may suggest that the ablative zones created by microwave ablation may be less affected by blood flow (the heat-sink effect).[14,20] The zone of active tissue heating in RF ablation is limited to a few millimeters surrounding the activated electrode, with the remainder of the tissue heated by thermal conduction.[16] Compared with RF, microwaves have a much broader field of power density up to 2 cm surrounding the antenna, with a correspondingly larger zone of active heating.[16] On the other hand, Shibata et al. have reported that the ablative zone size in microwave ablation is larger with blood flow interruption than without blood flow interruption in an in vivo experimental study.[21] This discrepancy may be attributable to the differences in the microwave systems employed.

Recently, a multiple RF electrode system that enables switching between three electrically independent electrodes at an impedance spike was created.[22] Compared with the single and cluster system used as controls, the multiple-RF ablation system enables the creation of significantly larger ablation zones. The benefit of microwave ablation system is that even more than three antennas can be activated simultaneously. We need to compare clinical efficacy between multiple RF ablation and multiple microwave ablation in the near future.

In conclusion, the results of the present ex vivo study clearly demonstrate that simultaneous microwave ablation using multiple microwave antennas creates large ablative zones without indentations when multiple antennas are activated with an antenna spacing of 2 cm or less.

References

1. Livraghi T, Goldberg SN, Lazzaroni S, Meloni F, Ierace T, Solbiati L, et al. Small hepatocellular carcinoma: treatment with radio-frequency ablation versus ethanol injection. Radiology 1999;210(3):655–61.
2. Yamakado K, Nakatsuka A, Ohmori S, Shiraki K, Nakano T, Ikoma J, et al. Radiofrequency ablation combined with chemoembolization in hepatocellular carcinoma: treatment response based on tumor size and morphology. J Vasc Intervent Radiol 2002;13(12):1225–32.
3. Takaki H, Yamakado K, Nakatsuka A, Fuke H, Murata K, Shiraki K, Takeda K. Radiofrequency ablation combined with chemoembolization for the treatment of hepatocellular carcinomas 5 cm or smaller: risk factors for local tumor progression. J Vasc Intervent Radiol 2007;18(7):856–61.
4. Liang P, Dong B, Yu X, Yu D, Wang Y, Feng L, et al. Prognostic factors for survival in patients with hepatocellular carcinoma after percutaneous microwave ablation. Radiology 2005;235(1):299–307.
5. Seki T, Wakabayashi M, Nakagawa T, Itho T, Shiro T, Kunieda K, et al. Ultrasonically guided percutaneous microwave coagulation therapy for small hepatocellular carcinoma. Cancer (Phila) 1994;74(3):817–25.
6. Shimada S, Hirota M, Beppu T, Matsuda T, Hayashi N, Tashima S, et al. Complications and management of microwave coagulation therapy for primary and metastatic liver tumors. Jpn J Surg 1998;28:1130–7.
7. Dong B, Liang P, Yu X, Su L, Yu D, Cheng Z, et al. Percutaneous sonographically guided microwave coagulation therapy for hepatocellular carcinoma: results in 234 patients. AJR 2003;180:1547–55.
8. Lu M, Chen J, Xie X, Liu L, Huang XQ, Liang LJ, et al. Hepatocellular carcinoma: US-guided percutaneous microwave coagulation therapy. Radiology 2001;221:167–72.
9. Yu NC, Lu DSK, Raman SS, Dupuy DE, Simon CJ, Lassman C, et al. Hepatocellular carcinoma: microwave ablation with multiple straight and loop antenna clusters. Pilot comparison with pathologic findings. Radiology 2006;239(1):269–75.
10. Simon CJ, Dupuy DE, Lannitti DA, Lu DS, Yu NC, Aswad BI, et al. Intraoperative triple antenna hepatic microwave ablation. AJR 2006;187:W333–40.
11. Shibata T, Iimuro Y, Yamamoto Y, Maetani Y, Ametani F, Itoh K, Konishi J. Small hepatocellular carcinoma: comparison of radio-frequency ablation and percutaneous microwave coagulation therapy. Radiology 2002;223(2):331–7.
12. Lu MD, Xu HX, Xie XY, Yin XY, Chen JW, Kuang M, et al. Percutaneous microwave and radiofrequency ablation for hepatocellular carcinoma: a retrospective comparative study. J Gastroenterol 2005;40(11):1054–60.
13. Ohmoto K, Yoshioka N, Tomiyama Y, Shibata N, Kawase T, Yoshida K, et al. Thermal ablation therapy for hepatocellular carcinoma: comparison between radiofrequency ablation and percutaneous microwave coagulation therapy. Hepatogastroenterology 2006;53(71):651–4.
14. Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. Radiographics 2005;25:s69–83.

15. Wright AS, Lee FT, Mahvi DM. Hepatic microwave ablation with multiple antennae results in synergistically larger zones of coagulation necrosis. Ann Surg Oncol 2003;10(3):275–83.
16. Wright AS, Sampson LA, Warner TF, Mahvi DM, Lee FT. Radiofrequency versus microwave ablation in a hepatic porcine model. Radiology 2005;236(1):132–9.
17. Hines-Peralta AU, Pirani N, Clegg P, Cronin N, Ryan TP, Liu Z, et al. Microwave ablation: results with a 2.45-GHz applicator in ex vivo bovine and in vivo porcine liver. Radiology 2006;239(1):94–102.
18. Mulier S, Ni Y, Frich L, Burdio F, Denys AL, De Wispelaere JF, et al. Experimental and clinical radiofrequency ablation: proposal for standardized description of coagulation size and geometry. Ann Surg Oncol 2007;14(4):1381–96.
19. Goldberg SN, Grassi CJ, Cardella JF, Charboneau JW, Dodd GD III, Dupuy DE, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. Radiology 2005;235(3):728–39.
20. Brace CL, Laeseke PF, Sampson LA, Frey TM, van der Weide DW, Lee FT Jr. Microwave ablation with a single small-gauge triaxial antenna: in vivo porcine liver model. Radiology 2007;242(2):435–40.
21. Shibata T, Niinobu T, Ogata N. Comparison of the effects of in-vivo thermal ablation of pig liver by microwave and radiofrequency coagulation. J Hepatobiliary Pancreat Surg 2000;7(6):592–8.
22. Laeseke PF, Sampson LA, Haemmerich D, Brace CL, Fine JP, Frey TM, et al. Multiple-electrode radiofrequency ablation creates confluent areas of necrosis: in vivo porcine liver results. Radiology 2006;241(1):116–24.