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Original Article

In Vivo Microwave Ablation of Normal Swine Lung at High-power, Short-duration Settings

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To evaluate the volume and heat-sink effects of microwave ablation (MWA) in the ablation zone of the normal swine lung. MWA at 100 W was performed for 1, 2, and 3 min in 7, 5, and 5 lung zones, respectively. We assessed the histopathology in the ablation zones and other outcome measures: namely, length of the longest long and short axes, sphericity, ellipsoid area, and ellipsoid volume. The mean long- and short-axis diameters were 22.0 and 14.1 mm in the 1-min ablation zone, 27.6 and 20.2 mm in the 2-min ablation zone; and 29.2 and 21.2 mm in the 3-min ablation zone, respectively. All measures, except sphericity, were significantly less with 1-min ablation than with either 2- or 3-min ablation. There were no significant differences between the 2- and 3-min ablation zones, but all measures except sphericity were larger with 3-min ablation. Although there were no blood vessels that resulted in a heat-sink effect within the ablation zones, the presence of bronchi nearby in 5 lung ablation zones resulted in reduced ablation size. In high-power, short-duration MWA, the lung ablation volume was affected by ablation time. Some ablations showed that a heat-sink effect by a neighboring bronchus might occur.

Key words: microwave ablation, lung, ablation zone, heat-sink effect, swine

Thermal ablation therapies, including radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation, are being used with high efficacy as less invasive treatment modalities for both primary and secondary lung cancers [1]. While RFA is still more common, the clinical use of MWA has been increasing [1]. However, the MWA protocol (*e.g.*, high or low power, long or short duration) has not yet been standardized. In addition, MWA can be performed using a variety of devices. A previous experimental study comparing the effects of four MWA devices on an *ex vivo* bovine liver showed significant differences between devices in ablation volume, sphericity, and short-axis diameter [2]. This issue complicates the matter of protocol standardization.

MWA can deliver faster and higher heating temperatures than RFA, making MWA treatments less susceptible to the heat-sink effect and able to produce larger ablation volumes [3-6]. MWA may be better for patients with larger numbers or sizes of tumors. The Emprint^{TM} Ablation System (Medtronic, Boulder, Co, USA), one of the newer next-generation MWA technologies [7], has recently been approved for liver can-

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cer. The Emprint^{TM} Ablation System is powered by a 2,450-MHz generator and can deliver a maximum power of 100 W. This technology yields predictable spherical zones of ablation, with the most predictable results achieved at 100 W [7,8]. The system has also been proven useful for delivering MWA to malignancies in other organs, such as the lung and kidney [9-11]. Only a few clinical reports have been published regarding the use of this device in the lung [10,11]. More animal and experimental studies are needed to understand how the Emprint^{TM} Ablation System can be used safely and effectively in patients with lung cancer. If high-power, short-duration MWA can achieve sufficient ablation volumes, this local therapy may offer a less invasive and more comfortable treatment modality than current lung cancer therapies.

The purpose of this study was to evaluate the volume and heat-sink effects in the ablation zones after using the Emprint^{TM} Ablation System with high power and short duration *in vivo* on normal swine lung.

Material and Methods

All animal experiments were conducted according to the institutional Policies and Guidelines for the Care and Use of Laboratory Animals, and all efforts were made to minimize animal suffering. This study was approved by the Institutional Animal Care and Use Committee (approval number, OKU-2019674).

Ablation procedure. Three female swine (weights, 41.6 kg, 43.9 kg, and 47.4 kg) were subjected to one-time ablation by the Emprint^{TM} Ablation System. The animals were sedated, and general anesthesia was maintained using continuous inhalation of isoflurane while MWA was performed in the swine lungs. The MWA antenna (13-gauge, 15-cm long) was inserted directly into the lung via the open chest by one interventional radiologist (T.I.) with 22 years of experience. In the three separate swine, MWA at 100 W was performed for 1, 2, or 3 min at 7, 5, and 5 lung sites, respectively.

After the ablation, a 22-gauge Surflo needle (Terumo Corporation, Tokyo, Japan) was inserted in parallel with the MWA antenna as a guide to mark the puncture route. The inner needle of the Surflo needle was removed, the outer tube remained, and the MWA antenna was removed.

Pathology analysis. One h after the MWA in the lung, the animal was euthanized. Both the lungs were immediately removed en bloc and fixed in 10% neutral buffered formalin and embedded in paraffin. The ablation zones were dissected along the outer tube of the Surflo needle, and tissues were prepared for histopathology. Tissue sections were cut at 4-μm thickness and stained with hematoxylin and eosin. The ablated region was identified by the following histological findings: -degeneration of the epithelium, edema, and hemorrhage of the stroma. A heat-sink effect was seen where the ablation size was diminished due to the buffering effect of patent blood vessels or ventilated bronchi adjacent to the ablation zone [12] (Fig. 1). The presence or absence of an apparent heat-sink effect based on qualitative examination was recorded for each zone. The lengths of the longest long and short axes of the ablated lesion were measured in each slide. All pathological analyses were performed by a board-certified pathologist with 12 years of experience (T.T.). This pathologist was blind to the duration of each ablation.

Statistical analysis. The outcome measures were i) length of the longest long axis, ii) length of the longest short axis, iii) sphericity, iv) ellipsoid area, and v) ellipsoid volume. The lengths of the longest long- and short-axis were measured directly. Sphericity was calculated by dividing the length of the longest short-axis by the length of the longest long-axis, with a value of 1 corresponding to a perfect sphere. Ellipsoid area was obtained by π×(radius of the longest long-axis)×(radius of the longest short-axis), and ellipsoid volume

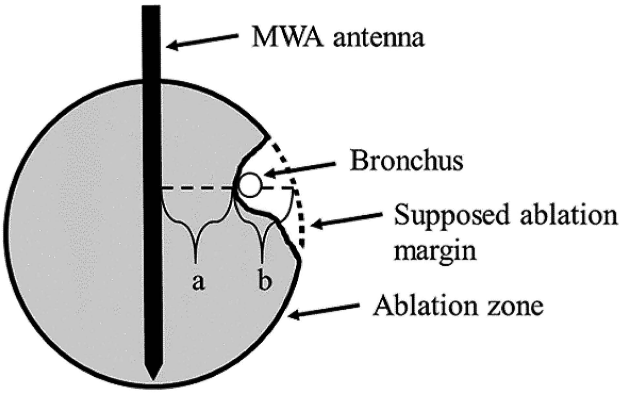

Fig. 1 Schema of the heat-sink effect caused by nearby bronchi. The presence of a bronchus nearby was associated with reduced ablation size (a, the distance between the MWA antenna and bronchus; b, the distance between the supposed and real ablation margin).

was 4/3 × π × (radius of the longest long-axis) × (radius of the longest short-axis) × (radius of the longest short-axis). The mean and standard deviation of outcome measures were calculated for each measurement. For pairwise comparisons of the 1-, 2-, and 3-min ablations of the lung, the Tukey-Kramer test was used.

P values < 0.05 were considered significant. Analyses were performed using Stata/MP4 version 16.1 (Stata Corp. College Station, TX, USA) by a statistician (T.M.) with 16 years of experience.

Results

Table 1 shows the results of descriptive statistics. In the 1-min ablation zone, the mean long-axis measurement was 22.0 mm while measures for the 2-min and 3-min were 27.6 mm and 29.2 mm, respectively (Fig. 2). The short-axis measurement was 14.1 mm in the 1-min zone, 20.2 mm in the 2-min zone, and 21.2 mm in the 3-min zone (Fig. 3).

The 1-, 2-, and 3-min lung ablations were compared using the Tukey-Kramer test. The long-axis diameters, short-axis diameter, ellipsoid area, and ellipsoid volume were significantly different between the 1- and 2-min ablation zones and the 1- and 3-min ablation zones (Table 2). There were no significant differences in outcomes between the 2- and 3-min ablation zones. Point estimates of differences of the means were small, ranging from −0.01 to 0.08. For sphericity, no significant differences were found in any comparison.

There were no blood vessels that resulted in a heat-sink effect within the lung ablation zones. The presence of a neighboring bronchus (median diameter, 3 mm; range, 1-5 mm) in 5 of the 17 lung ablation zones seemed to result in reduced ablation size (Table 3 and Fig. 4).

Table 1 Outcome measures of each ablation

Ablation time		The longest long axis (mm)	The longest short axis (mm)	Sphericity	Ellipsoid area (mm^2)	Ellipsoid volume (mm^3)
1 min (n = 7)	Mean	22.0	14.1	0.65	245.3	2,418.1
	SD	3.2	3.2	0.18	68.4	1,018.1
	Range	17–26	8–18	0.40–0.90	125.7–326.7	670.2–3,484.9
2 min (n = 5)	Mean	27.6	20.2	0.73	438.4	5,982.7
	SD	1.8	2.5	0.09	65.6	1,606.4
	Range	25–30	17–24	0.63–0.86	360.5–527.8	4,085.4–8,444.1
3 min (n = 5)	Mean	29.2	21.2	0.73	497.6	7,368.9
	SD	5.2	3.9	0.06	167.3	3,475.2
	Range	24–36	16–24	0.67–0.80	301.6–678.6	3,216.8–10,856.8

SD: standard deviation.

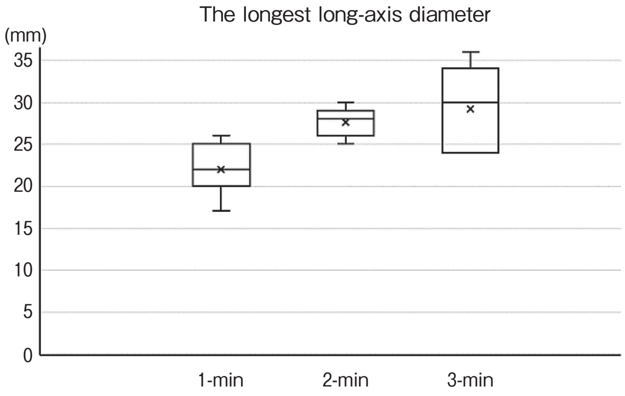

Fig. 2 The longest long-axis diameter of each ablation.

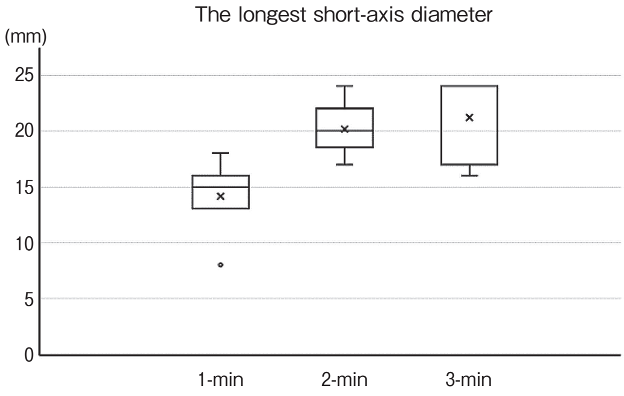

Fig. 3 The longest short-axis diameter of each ablation.

Table 2 Tukey's test results comparing 1-, 2-, and 3-minute ablation zones in healthy swine lung

		Difference of the mean	95% CI	*P* value
The longest long axis (mm)	2 min vs 1 min	5.60	0.04, 11.16	0.048
	3 min vs 1 min	7.20	1.64, 12.76	0.011
	3 min vs 2 min	1.60	−4.40, 7.60	0.769
The longest short axis (mm)	2 min vs 1 min	6.06	1.07, 11.05	0.017
	3 min vs 1 min	7.06	2.07, 12.05	0.006
	3 min vs 2 min	1.00	−4.39, 6.39	0.879
Sphericity	2 min vs 1 min	0.08	−0.12, 0.28	0.576
	3 min vs 1 min	0.07	−0.13, 0.28	0.629
	3 min vs 2 min	−0.01	−0.23, 0.21	0.996
Ellipsoid area (mm^2)	2 min vs 1 min	193.14	30.70, 355.58	0.020
	3 min vs 1 min	252.36	89.92, 414.80	0.003
	3 min vs 2 min	59.22	−116.24, 234.67	0.659
Ellipsoid volume (mm^3)	2 min vs 1 min	3,564.62	266.31, 6,862.92	0.034
	3 min vs 1 min	4,950.79	1,652.49, 8,249.09	0.004
	3 min vs 2 min	1,386.18	−2,176.40, 4,948.75	0.578

CI: confidence interval.

Table 3 Summary of heat-sink effect of bronchi in lung ablation

		Ablation diameter			Distance		
Case	Ablation time (min)	The longest long-axis (mm)	The longest short-axis (mm)	Maximum bronchus diameter (mm)	Between antenna and bronchus (mm)	Between supposed and real ablation margin (mm)	Pathological change of bronchus affected ablated area
1	1	25	13	2	4	4	Loss of cilia with flattening of epithelium
2	1	20	18	2	7	2	None
3	2	28	24	3	6	4	None
4	3	24	16	1	4	5	Loss of cilia with flattening of epithelium
5	3	30	24	5	8	6	None

Discussion

This study showed a correlation between ablation volume and the ablation duration in MWA using the Emprint^{TM} Ablation System at high power (*i.e.*, 100 W) for a short duration (*i.e.*, 1, 2, and 3 min). Sphericity was not significantly different among the zones. Some lung ablations showed that the presence of bronchi in the ablation zone may cause a heat-sink effect, effectively reducing the ablation zone.

In an animal study that compared ablations of 2- and 10-min durations using the same MWA device as ours, on the same high-power (*i.e.*, 100 W) setting, the computed tomography (CT) findings at day 0 showed that the swine lung ablation size from the long ablation duration was significantly larger than that from the short ablation duration [13]. This trend was also observed in our study within a much shorter ablation duration, although there was no significant difference between the 2- and 3-min ablations. Another result from their study was that a longer duration of energy delivery produced significantly more spherical zones of ablation than shorter durations. [13]. No significant differences in sphericity were noted among our three groups, possibly because of the small differences among the short durations (*i.e.*, 1 vs. 2 vs. 3 min) or because of the small number of samples (7, 5 and 5 ablation zones). However, because our protocol (*i.e.*, high power and short duration) achieved a sufficient ablation volume, this protocol may be applicable depending on the target tumor diameter.

Kodama *et al.* performed 18 percutaneous MWA

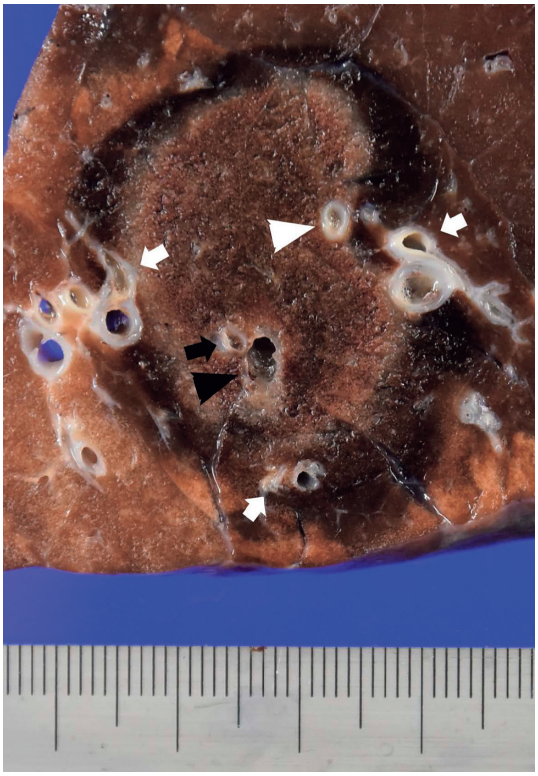

Fig. 4 Case of a neighboring bronchus associated with a reduced ablation size. Gross image after 2-min MWA shows the ablation zone (the longest long-axis diameter, 28 mm; the longest short-axis diameter, 24 mm) in the lung. The MWA antenna (black arrowhead), pulmonary artery (small white arrow) and pulmonary vein (small black arrow) can be seen within the ablation zone. The ablation margin is apparently depressed 4 mm inward by the presence of a bronchus with a diameter of 3.0 mm (white arrowhead).

procedures using the same Emprint^{TM} Ablation System on normal swine lungs at 100 W for 2 min, and their results showed a significant peak in the post-ablation zone volumes on day 7 [14]. They also reported no significant differences in the ablation zone size between CT and gross pathologic images [14]. Although our lung ablation measures for 2-min application were slightly larger than their results on day 0, the comparison may be affected by the smaller number of our ablations (n = 5) compared to theirs (n = 18).

The heat-sink effect is a well-established phenomenon in both animal studies and clinical applications of lung RFA [15-17]. In the clinical setting, RFA is less effective when the lung tumor is adjacent to a large vessel of ≥ 3 mm or a bronchus of ≥ 2 mm in diameter [16, 17]. Presumably because of its higher temperatures and shorter ablation times, MWA is less susceptible to the heat-sink effect than other heat-based ablation modalities [6, 18, 19]. However, in five ablation zones with nearby bronchi (median diameter 3 mm; range 1-5 mm), a reduced ablation size was seen. Indeed, the heat-sink effect by air might be greater than that by vessels. In a swine study using other MWA devices, a vessel or bronchus of < 6 mm did not affect ablation size or sphericity, whereas a heat-sink effect was observed for larger vessel diameters [20]. In contrast, another swine study using the same Emprint^{TM} Ablation System found that the presence of large airways or blood vessels did not result in a heat-sink effect within the lung ablation zones and was not indicative of reduced ablation size. However, all bronchi and blood vessels within their ablation zones were completely necrotic, regardless of size and duration of energy delivery [13]. They performed repeated high-power (100 W) MWA of short (2 min, 18 ablations) or long duration (10 min, nine ablations) under CT guidance. Unlike their study, we performed one-time ablation, and directly inserted a smaller number of antennas into the open chest without recognizing bronchial or vascular localization in the lung, which may explain the different results between the studies. Operators should be aware that the heat-sink effect can occur during high-power, short-duration MWA of the lung, even if high-power, short-duration MWA is less susceptible to this effect than other modalities [6].

Several animal studies have evaluated the ablation zone using other MWA devices, including various models (*e.g.*, *in vivo*, *ex vivo*, normal lung, and lung tumor mimic). Planché *et al.* reported results from a tumor mimic model using another MWA device at 75 W and 15 min in an *in vivo* swine lung. They found that the longest long- and short-axis mean diameters were 35.7 mm and 32.7 mm, respectively [20]. Gao *et al.* reported results using a different MWA device for 2 min in an *ex-vivo* porcine lung; they found the longest long- and short-axis mean diameters were 16.3 mm and 13.4 mm at 30W; 22.9 mm and 19.1 mm at 40W; and 28.5 mm and 22.0 mm at 50 W [21]. The lung ablation volumes may be different for each MWA device, similar to previous results from the liver [2]. However, it is difficult to compare results across various powers and duration times. It would be helpful to compare lung ablation zones created by various MWA devices under the same conditions.

Our study had several limitations. Ablations were performed in healthy swine lungs, not on those with tumors. Only one MWA device (*i.e.*, Emprint^{TM} Ablation System) was used. Therefore, it is unclear whether the same results would be achieved on other devices. The lengths of the longest long- and short-axes of the ablated lesion were measured on a per-slide basis, and the heat-sink effect was evaluated. However, a three-dimensional assessment might have been preferable to this two-dimensional approach. Additionally, it is unclear whether the volume of blood vessels and bronchi/lung volume were constant throughout this study.

In conclusion, the ablation volume of the lung was affected by ablation time. Some ablation zones from MWA using the Emprint^{TM} Ablation System at high-power and short-duration settings were apparently affected by the presence of a bronchus as a heat sink.

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