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ORIGINAL ARTICLE

Discontinuous moving shot technique for conformal thermal ablation in an *ex vivo* porcine liver model

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PURPOSE
We aimed to determine the ablation characteristics of discontinuous moving shot technique (DMST) in microwave ablation (MWA), radiofrequency ablation (RFA) and laser ablation (LA), and analyze the differences compared with fixed electrode technique (FET) in an *ex vivo* porcine liver model.

METHODS
FET was defined as the ablation needle remaining fixed during ablation. In DMST, ablation needle moved backward for a fixed distance twice along the long axis during ablation. Four moving distances (0.5 cm, 0.75 cm, 1 cm and 2 cm) were used in DMST. Long-axis diameter (LAD) and short-axis diameter (SAD) of ablation zones were measured. The ratio of LAD/SAD was calculated.

RESULTS
The shape and size of ablation zones were different between DMST and FET. Compared with FET, DMST could achieve greater LAD when the moving distance became long enough. In MWA with DMST, SAD decreased with the extension of moving distance and finally became smaller than the SAD in FET. While in LA and RFA, the change of moving distance did not affect SAD significantly.

CONCLUSION
In MWA, RFA and LA, the characteristics of ablation zone of DMST were different from that of FET. This unique ablation technique may be suitable for conformal thermal ablation.

Thermal ablation therapies, including radiofrequency ablation (RFA), microwave ablation (MWA) and laser ablation (LA), have been widely used in the treatment of solid tumors (1–5). Usually, fixed electrode technique (FET) is used in tumor ablation therapy, with the electrode in the central portion of the tumor and remaining fixed during the entire ablation time (6). This will create a large round ablation zone, including the whole tumor and part of surrounding normal tissue, to obtain sufficient safety margin (5, 7, 8).

In the clinical practice of thermal ablation of solid tumors, surgeons often encounter tumors which are elliptical in shape (9–11). At this point, if FET is adopted, surgeons need to increase the ablation power or time to create an ablation zone with a greater long axis. At the same time, the short axis of ablation zone will be much greater than is needed, and this can easily damage surrounding normal tissues (12, 13). Therefore, we need a more flexible and conformal ablation technique which can easily adjust the long axis and short axis to make the ablation range more suitable for the tumor lesion. Previous studies (10, 14–16) have suggested moving shot technique (MST) for RFA in the treatment of thyroid nodules, and achieved successful clinical outcomes. Effective MWA using MST has also been reported in the treatment of benign breast lesions (17, 18). MST may be more suitable for accurate and conformal thermal ablation than FET. By moving the ablation needle, it can create an ablation zone that conforms to the tumor lesion. However, MST is not easy to perform because the moving of ablation needle is continuous and it is difficult for operators to keep the moving speed steady and uniform (10, 17). If the operator moves ablation needle too fast, it can easily cause incomplete ablation. Studies have shown that incomplete ablation may promote tumor progression (19–21). In this study, we reported a different ablation

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technique, discontinuous moving shot technique (DMST), in MWA, RFA and LA. The ablation characteristics of DMST were compared with that of FET in the three kinds of thermal ablation using an *ex vivo* porcine liver model. Furthermore, the influence of moving distance in this technique was analyzed.

Methods

Due to no live animals used, our study was exempt from the Animal Care and Use Subcommittee at our university. Fresh adult porcine livers were procured from a local slaughterhouse. The livers were cut into 10×5×5 cm^3 blocks, each of which was large enough for one ablation. In the process of cutting liver blocks, vessels larger than 6 mm were avoided by using ultrasound as in a previous study (22). Ablation needle was inserted into the center of liver block along the long axis. The liver blocks were bathed in water at 37°C for 30 minutes before ablation and during the whole process of ablation. All thermal ablation procedures were performed by surgeons with 8 years of experience in thermal ablation.

Equipment of MWA, RFA and LA

The microwave system (ECO-100E, Yigao Microwave Electric Institute) used in this study consists of a microwave generator, a flexible coaxial cable, a water-pumping machine and a needle antenna. The cooled-shaft antenna was 2 mm in diameter and had a 2 mm long irradiating segment embedded in the front of the needle. Its irradiation frequency was 2450 MHz and the output power selected in this study was 40 W.

A 480 KHz radiofrequency generator (S-5L, MedSphere International) with a maximum power output of 50 W was applied. We used a 16-gauge cooled-shaft monopolar electrode with stainless steel tip exposure of 1 cm. A metallic pad was attached to the lateral wall of the bath. The output power of RFA in this study was 20 W.

LA system used in our research was a four-channel LA system (Echolaser X4, EL.EN SPA). The wavelength of the laser was 1064 nm and the energy was delivered with a laser fiber which is connected to the channel; the diameter of the fiber was 0.3 mm. The output power selected in LA was 7 W.

Main points

- Compared with fixed electrode technique (FET), discontinuous moving shot technique (DMST) could achieve greater long-axis diameter when the moving distance became long enough.
- In microwave ablation with DMST, short-axis diameter (SAD) decreased with the extension of moving distance and finally became smaller than the SAD in FET.
- In laser and radiofrequency ablations, the change of moving distance did not affect SAD significantly.

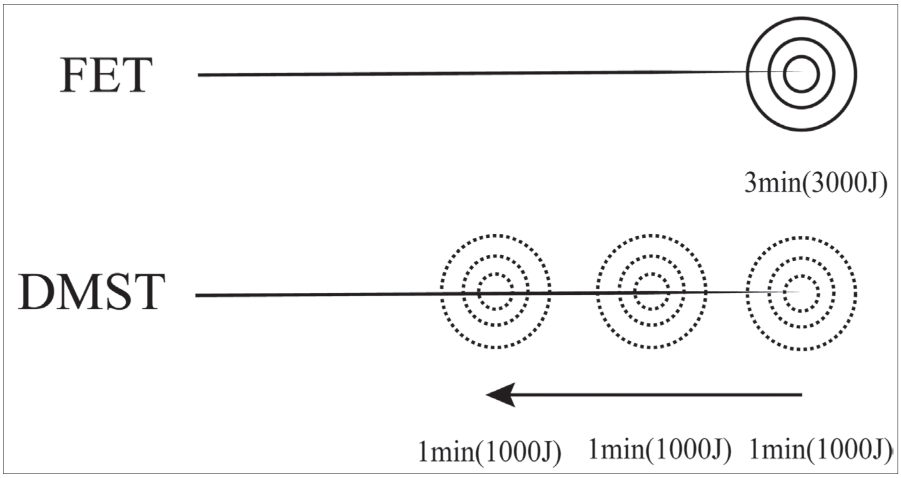


Figure 1. Schematics showing the definitions of fixed electrode technique (FET) and discontinuous moving shot technique (DMST) used in this study.

Procedure of FET in MWA, RFA and LA

FET was defined as the ablation needle remaining in a fixed position during ablation (Fig. 1). The inserting depth of ablation needle was 5 cm in FET. Using FET, MWA and RFA were performed for 3 minutes. LA with FET was performed for 3000 joules. Each group included 10 ablations in 10 liver blocks, respectively.

Procedure of DMST in MWA, RFA and LA

DMST was defined as the ablation needle moving backward for a fixed distance twice along the long axis during the entire ablation time (Fig. 1). The inserting depth of DMST was 7 cm. Each type of thermal ablation in DMST was divided into 4 groups according to the moving distances of 0.5 cm, 0.75 cm, 1 cm and 2 cm. Each group included 10 ablations in 10 liver blocks, respectively. In MWA and RFA, the ablation time used before moving and after each movement was 1 minute. In LA, the ablation energy applied before moving and after each movement was 1000 joules.

Examination of the ablation specimens

After each ablation, the ablation zone was sectioned along the track of ablation needle. The border of coagulation zone was verified by histochemical staining with α-nicotinamide adenine dinucleotide, reduced (NADH)-diaphorase. The shape and size of ablation zones were determined based on α-NADH-diaphorase staining. The maximum long-axis diameter (LAD) parallel to the needle and the maximum short-axis diameter (SAD) perpendicular to the needle were measured. The diameters were evaluated independently by two pathologists with more than 10 years of experience in pathologic examination. The ratio of LAD/SAD was calculated.

Statistical analysis

Numerical data were recorded as mean ± standard deviation (SD). One-way analysis of variance was applied to identify the differences of LAD, SAD, and LAD/SAD among different groups. Post hoc test was performed with Bonferroni correction. All statistical analyses were performed by using software (Stata version 11.0; StataCorp), and a significant difference was accepted for $p < 0.05$.

Results

Due to the phenomenon of radiofrequency cutoff, the actual ablation time of FET in RFA did not reach 3 minutes. We recorded the actual ablation time and corresponding ablation energy (mean±SD, 68.10±3.35 s and 1362±66.97 joules). Cutoff phenomenon was not observed in DMST for RFA. All the variables of ablation zones were shown in the Table.

Table. Variables of MWA, RFA and LA using DMST

	MWA					RFA					LA				
Moving distance (cm)	0	0.50	0.75	1.00	2.00	0	0.50	0.75	1.00	2.00	0	0.50	0.75	1.00	2.00
Time for ablation (s)	180	180	180	180	180	68.10±3.35	180	180	180	180	428.57	428.57	428.57	428.57	428.57
Energy (J)	7200	7200	7200	7200	7200	1362.00±66.97	3600	3600	3600	3600	3000	3000	3000	3000	3000
LAD (mm)	40.10±2.02	28.50±2.42	34.50±1.35	42.80±2.94	60.30±4.22	17.70±2.00	27.40±2.12	32.20±1.48	36.60±1.17	42.60±2.76	40.00±2.49	24.70±1.06	32.20±2.30	35.20±1.75	49.60±3.06
SAD (mm)	21.40±2.22	21.70±1.49	21.50±1.08	19.20±1.23	12.60±1.17	13.30±0.95	14.90±1.37	13.90±1.37	12.80±1.14	12.20±0.79	17.10±1.37	13.50±0.71	12.30±0.82	11.40±1.17	11.60±0.97
LAD/SAD	1.89±0.18	1.32±0.15	1.61±0.11	2.24±0.27	4.83±0.62	1.33±0.13	1.86±0.29	2.34±0.30	2.88±0.28	3.50±0.28	2.35±0.24	1.83±0.12	2.63±0.22	3.11±0.27	4.31±0.48
p^a	-	<0.001	<0.001	1.000	<0.001	-	<0.001	<0.001	<0.001	<0.001	-	<0.001	<0.001	0.001	<0.001
p^b	-	1.000	1.000	0.014	<0.001	-	0.674	1.000	1.000	1.000	-	<0.001	<0.001	<0.001	<0.001
p^c	-	0.001	1.000	0.749	<0.001	-	0.004	<0.001	<0.001	<0.001	-	0.006	1.000	<0.001	<0.001

MWA, microwave ablation; RFA, radiofrequency ablation; LA, laser ablation; DMST, discontinuous moving shot technique ; LAD, long-axis diameter; SAD, short-axis diameter; FET, fixed electrode technique.
[a]Comparison of LAD between DMST and 3-minute FET in MWA and RFA (3000-joule FET in LA).
[b]Comparison of SAD between DMST and 3-minute FET in MWA and RFA (3000-joule FET in LA).
[c]Comparison of LAD/SAD between DMST and 3-minute FET in MWA and RFA (3000-joule FET in LA).

Clear and sharp boundaries could be observed in all three types of thermal ablation, and α-NADH-diaphorase staining confirmed that the boundaries separated thermally inactivated cells from surrounding viable cells (Fig. 2).

In ablation with FET, all the ablation zones were elliptic. In ablation with DMST, the ablation zones were elliptic when the moving distance was relatively short (0.5 cm, 0.75 cm and 1 cm). But when the moving distance reached 2 cm, the ablation zone became an irregular strip in MWA, and it turned into three separate ellipses in RFA and LA (Figs. 3 and 4).

In the three types of thermal ablation with DMST, LAD increased with the extension of moving distance, and it finally exceeded the LAD in FET (Fig. 5). In RFA, the LAD of 0.5 cm DMST was significantly larger than that of FET. But in MWA and LA, when the moving distance was relatively short, the LAD was significantly shorter than that of FET (0.5 cm and 0.75 cm in MWA; 0.5 cm, 0.75 cm and 1 cm in LA) (Table).

By comparing in pairs, we found that the SAD of MWA decreased with the extension of the moving distance. But in RFA and LA with DMST, the extension of moving distance did not affect the SAD of ablation zone significantly (Fig. 5). Furthermore, we compared the SAD of FET and DMST in the three types of thermal ablation. In MWA, when the moving distance was relatively short (0.5 cm and 0.75 cm), SAD was not significantly different compared with FET. But with the extension of moving distance, the SAD of DMST finally became shorter than that of FET. In RFA, SAD was not significantly different between DMST and FET. In LA, the SAD of DMST was smaller than that of FET under all four moving distances (Table).

In the three types of thermal ablation with DMST, the LAD increased with the extension of moving distance while the SAD decreased or did not change significantly, such that the ratio of LAD/SAD increased gradually (Fig. 5d). Compared with FET, DMST could achieve a greater ratio of LAD/SAD in the three types of thermal ablation (Table).

Discussion

In the ablation using DMST, the change of LAD could be explained by two factors. The first factor was moving distance. The ablation needle moved along the long axis, so the LAD would increase as the moving

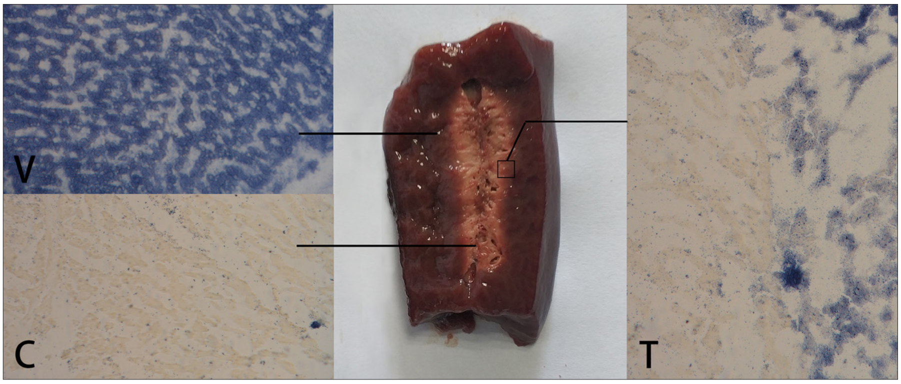


Figure 2. α-NADH-diaphorase staining images in a representative ablated liver sample with radiofrequency ablation (RFA) shows the macroscopic boundary separating thermally inactivated cells from surrounding viable cells. Surrounding viable cells are stained blue. The coagulation zone is stained negative. Similar α-NADH-diaphorase staining results were observed in microwave ablation (MWA) and laser ablation (LA) (data not shown). Original magnification, ×10; V, viable cells; C, coagulation zone; T, transition zone.

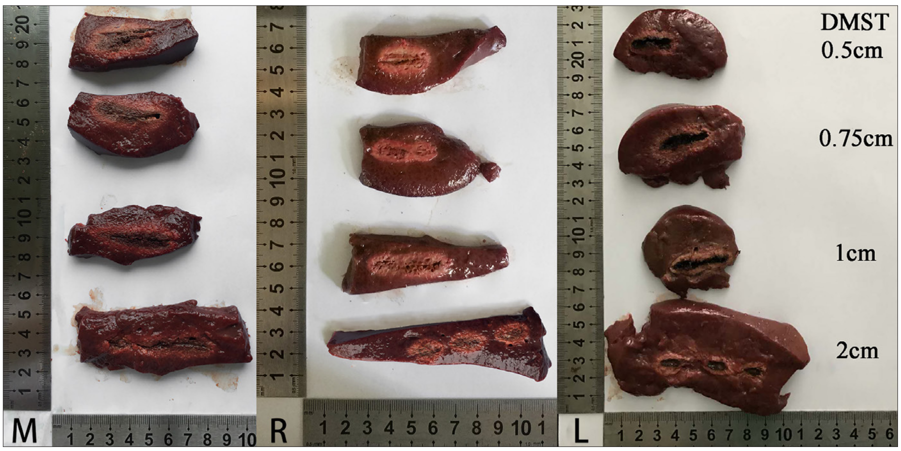


Figure 3. Ablation zones of MWA (M), RFA (R) and LA (L) using DMST were excised for measurement.

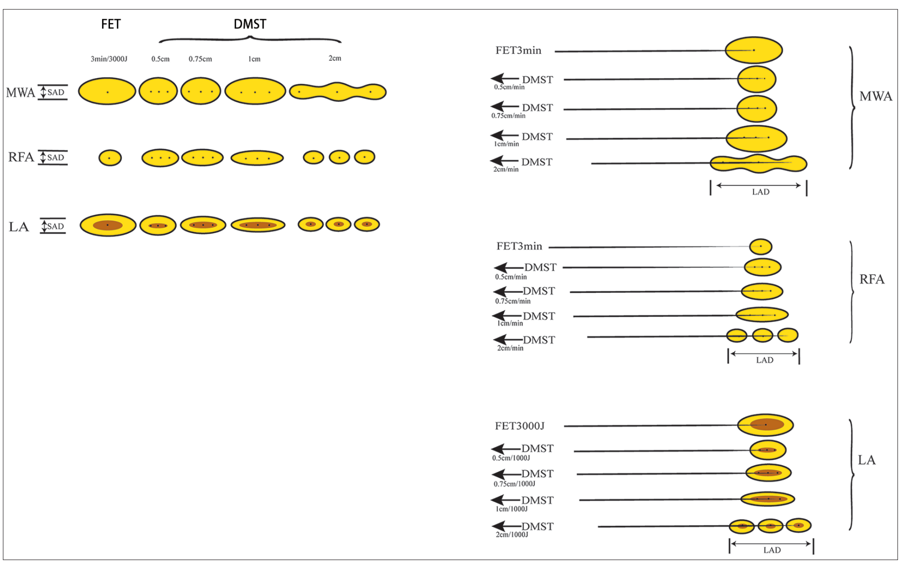
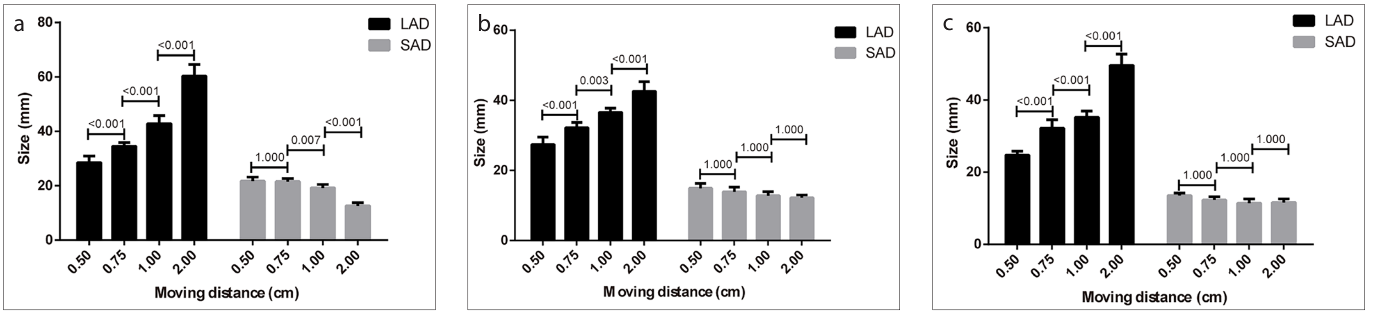


Figure 4. Diagram of ablation areas in MWA, RFA, and LA using FET and DMST.

distance became longer. The second factor was the overlap effect of ablation. During the ablation using FET, which could be regarded as having a moving distance of 0 cm, the overlap effect should be the most obvious. With the extension of moving distance, the overlap effect is weakened. In MWA and LA, when the moving distance was relatively short (0.5 cm and 0.75 cm in MWA; 0.5 cm, 0.75 cm and 1 cm in LA), the moving factor had a relatively small impact on LAD, while the attenuation of overlap effect mainly contributed to the decrease of LAD compared with FET. However, as the moving distance increased, the moving factor became prominent while the overlap effect was weakened. Therefore, the LAD of MWA and LA with DMST finally exceeded that of FET. In RFA with DMST, the actual ablation time was obviously longer than that of FET because of the avoidance of radiofrequency cutoff. In addition to moving distance and overlap effect, this was another factor that could increase the LAD of DMST in RFA.

In the three types of thermal ablation with DMST, the changes of SAD were different. This indicated that the overlap effect on SAD was different during different kinds of ablation. In MWA and LA, the SAD of DMST could become significantly shorter than that of FET. However, in RFA, there was no significant difference in SAD between DMST and FET. In other words, the increased actual ablation time in RFA with DMST did not result in corresponding increase in SAD compared with FET. This suggested that RFA with DMST had the least obvious overlap effect among the three kinds of thermal ablation. The difference in the overlap effect on SAD between MWA, LA and RFA may be related to the mechanism of heat production. MWA uses electromagnetic energy to rapidly rotate adjacent polar water molecules to produce frictional heat. In LA, the laser emitted by the fiber tip penetrates and scatters around the surrounding tissue, generating heat which leads to subsequent thermal damage. RFA uses a high frequency alternating electrical current to create ionic agitation to produce heat. During RFA, carbonization of tissue will cause exponential rising electrical impedances, which will obviously inhibit further ablation (23). A previous study has shown that MWA had several advantages over RFA, including higher intratumoral temperatures and larger ablation volumes (6). LA has also been reported to produce higher temperature and cause larger lesion volumes compared with RFA (24). Therefore, the characteristics of heat production in RFA may account for the less overlap effect on SAD compared with MWA or LA. Moreover, the ablation needle of RFA moved backward during ablation with DMST, allowing the tissue around the tip of ablation needle to maintain a situation of low impedance and thus avoiding the phenomenon of radiofrequency cutoff.



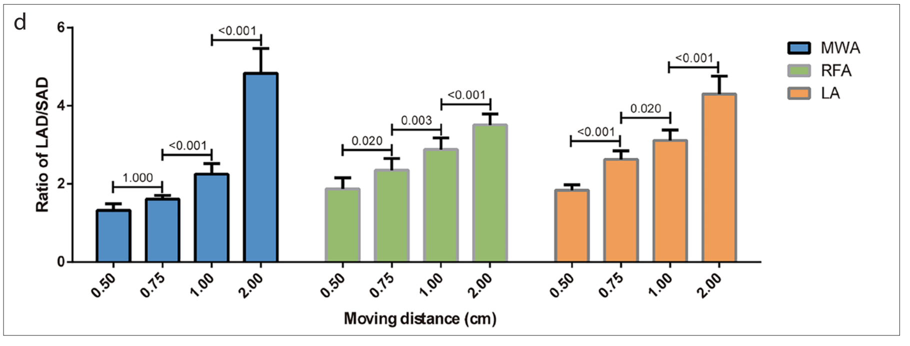


Figure 5. a–d. Post hoc tests for LAD and SAD in MWA **(a)**, RFA **(b)** and LA **(c)** using DMST were shown in the histograms. Panel **(d)** shows the comparison of LAD/SAD ratios using DMST in MWA, RFA and LA.

DMST in this study may be more suitable for conformal thermal ablation than traditional FET. With DMST, the LAD of ablation zone can be flexibly adjusted by modulating the moving distance. Meanwhile, the SAD could decrease or keep unchanged by choosing different types of thermal ablation. This can make the ablation range more suitable for the shape of tumor, especially for elliptic tumor lesions with large LAD/SAD ratios.

This study has several shortcomings. First, porcine livers without tumors were used for ablation. But animal livers bearing tumors are difficult to obtain. Excised animal liver is a common specimen for studying ablation zone. Previous studies (6, 7) used *in vitro* ablation in animal liver models to determine the size and shape of ablation zones. So the *ex vivo* porcine liver model in this study may reflect the ablation characteristics to some extent and help us understand the difference between DMST and FET more intuitively. Second, our study did not have *in vivo* results. Accordingly, the *in vivo* environment was simulated in the porcine liver model. For example, we used constant temperature water bath to simulate the temperature and humidity *in vivo*. Of course, further *in vivo* studies are still needed to validate our findings.

In conclusion, DMST may be suitable for conformal thermal ablation using RFA, MWA and LA, and the characteristics of the three kinds of thermal ablation with DMST were different from that with FET. Future studies are still needed to confirm these results.

Financial disclosure

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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