Ph.D. Dissertation of Medicine

Development of multi-purpose electrodes for radiofrequency ablation to maximize ablation effect and prevent thermal injury

열손상 방지 및 절제 효과 극대화를 위한 고주파 절제용 다목적 전극 개발

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Abstract

Keyword: Radiofrequency ablation; Octopus MP electrode; Conventional electrode; Ablation volume; Thermal injury
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Objective: To evaluate the feasibility, ablative zone, and safety of radiofrequency ablation (RFA) using Octopus multipurpose (MP) electrodes in ex vivo and in vivo porcine liver.
Materials and Methods: A total of 4 experiments were conducted in the ex vivo study. Experiments A and B compared the ablation performance with the conventional electrode and compared the performance according to the exposure length variation (20mm, 25mm, 30mm). In Experiment C, the effect of the temperature sensing electrode was verified. The output was terminated when the temperature reached 60 degrees during ablation, and it was assumed that there was an organ that should not be thermally damaged at a distance of 10 mm around the target electrode. Experiment D tested the difference in performance according to saline injection. A multipurpose electrode was inserted into the center of the two electrodes, and saline was injected for 3 minutes from 3 minutes after ablation, and the performance was compared.
In in vivo study, total 16 pigs were used. RFA was performed in the liver for 6 min using the Octopus MP electrodes and the conventional electrodes to investigate the effect of saline instillation in the first experiment. Ablation energy, electrical impedance, and ablation volume were compared between the two groups. RFA was performed near the gallbladder (GB) and colon using the Octopus MP electrodes with direct tissue temperature monitoring and the conventional electrodes in the second experiment. RFA was discontinued when the temperature was increased to > 60° C in the Octopus MP electrode group, while RFA was performed for a total of 6 min in the conventional electrode group. Thermal injury was assessed and compared between the two groups upon pathological examination.
Results: When comparing the conventional electrode and the Octopus MP electrode in the ex vivo study, there was no statistically significant difference between the two electrodes in terms of change according to exposure length and performance in experiment A and B. In Experiment C, which compared performance according to temperature measurement, the total energy and ablation volume were statistically significantly lower than the

conventional electrode group that did not measure temperature (P <0.001, respectively). The group injected with saline had a statistically significantly lower impedance than the non−injected group, and the total energy and ablation volume were higher (P<0.001, respectively) in experiment D.
In the first experiment of in vivo study, the ablation volume and total energy delivered in the Octopus MP electrode group were significantly larger than that in the conventional electrode group (15.7±4.26 cm3 vs. 12.5±2.14 cm3, P=0.027; 5.48±0.49 Kcal vs. 5.04±0.49 Kcal, P=0.029). In the second experiment, thermal injury to the GB and colon was less frequently noted in the Octopus MP electrode group than in the conventional electrode group (16.7% (2/12) vs. 90.9% (10/11); 8.3% (1/12) vs. 90.9% (10/11), P<0.001 for all). The total energy delivered around the GB (2.65±1.07 Kcal vs. 5.04±0.66 Kcal) and colon (2.58±0.57 Kcal vs. 5.17±0.90 Kcal) were significantly lower in the Octopus MP electrode group than in the conventional electrode group (P<0.001 for all).
Conclusion: RFA using the Octopus MP electrodes is capable of saline instillation and direct tissue temperature measurement, and induces a larger ablation volume and results in lesser thermal injury to the adjacent organs compared with conventional electrodes.

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Chapter 1. Introduction

1.1. Study Background

Radiofrequency ablation (RFA) is a potentially curative treatment for early-stage hepatocellular carcinoma (HCC) and a bridging therapy for patients awaiting liver transplantation [1-5]. Additionally, RFA is preferred over surgical resection for very early-stage HCC (single HCC < 2 cm), according to the Barcelona Clinic Liver Cancer Staging and Treatment Strategy Guidelines [5]. However, one of the major drawbacks of RFA is the high rate of local tumor progression (LTP) compared with that of surgical resection [6,7]. An important factor related to this limitation is the concentration of high-frequency current within 5 mm of the tissue around the electrode that causes an excessive increase in the impedance and charring around the electrode during RFA [8-10]. Moreover, a typical lesion created by a linear RF electrode is elliptical in shape, with the major axis parallel to the electrode shaft [10]. However, malignant liver tumors could present irregular shapes rather than spherical or oval shapes, and controlling the short axis of the ablation zone to ensure complete ablation while minimizing unnecessary loss of functional hepatic parenchyma remains a challenge [11]. In addition, because RFA can ablate not only tumors but also adjacent liver parenchyma, complications may occur in the gallbladder (GB), biliary tract, stomach, and colon [12,13]. Therefore, while the creation of ablation zones conformable to the tumor index and safety margin is warranted, decreasing unnecessary thermal damage to adjacent vital structures is also considered crucial.

Considering studies on improving the efficiency of RF devices for creating ablation zones, several reports showed that an internally cooled wet electrode capable of perfusion of saline into the tissue during RFA could create a large ablation zone compared to conventional RF electrodes [14-16]. However, these perfusion electrodes have the risk of irregularly shaped ablation, distal heating, and ablation of non−tumor−containing areas; moreover, there is a possibility of organ damage if the tumor is located in the subcapsular region or adjacent to other internal organs [17,18]. In clinical practice, a large ablation zone with a perfusion electrode is not always beneficial for the management of malignant liver tumors [11].

1.2. Purpose of Research

Therefore, to improve the efficiency of creating a large ablation zone while preventing damage to adjacent organs, we developed new electrodes (Octopus multipurpose [MP]) that are composed of two separable electrodes with an adjustable active tip and a thin applicator with open holes, capable of both saline instillation and temperature measurements. In this study, we aimed to compare Octopus MP electrodes and conventional electrodes for RFA in porcine livers in vivo.

Chapter 2. Materials and Methods

1.1. The RFA Equipment

A multichannel RF system was employed to deliver the RF energy in single−switching monopolar mode using two electrodes. RF energy (maximum 200 W) was applied to one of the two electrodes, which was switched between the two electrode tips of the separable clustered electrode based on tissue impedance changes. The new RF electrodes, Octopus MP (Octopus electrode; STARmed), used a thin applicator with open holes capable of both saline instillation (19 gauge) and temperature measurements and two internally cooled electrodes (17 gauge). These cooled electrodes had a 2.5−cm long adjustable active tip (Fig. 1) that can be used by adjusting the active tip length according to the size of the target. The saline applicator/temperature probe does not participate in active ablation (Fig. 1). Temperature sensing monitors the actual temperature of probe and measures the temperature displayed in the multichannel RF system.

Since the impedance rise starts 2 minutes after the start of ablation, chilled normal saline was infused into the lumen of the applicator to lower the impedance at a rate of 0.5 mL/1 min from minute 2 until the end of the ablation (6 minutes). A peristaltic pump (VIVA Pump; STARmed) was used to keep the tip temperature below 25° C. Technical parameters, including the average power output, electrical impedance, applied current, and total energy delivered, were continuously monitored, and recorded using monitoring software (VIVA Monitor Software V 1.0; STARmed).

1.2. Ex vivo study

Freshly extracted porcine livers were transported to our research laboratory immediately before the experiment and were partially immersed in saline−filled bath. A custom−made metal plate grounding pad was placed to one sidewall of the bath. The RF electrode was inserted on the outer hepatic capsule into the liver parenchyma at the same depth (4-5 cm). A total of four types of experiments were planned and executed at room temperature.

1.3. Experiment A: Verification of performance according to varying exposure length

Experiments were conducted in automatic mode with an output of 200 watt and the active tip of the electrode is changed to 20mm, 25mm, and 30mm respectively. In the Octopus MP electrodes, the active tip was selected while varying the exposure length, and in the conventional electrode, 20mm, 25mm, and 30mm electrodes of 17 gauge were used for the experiment. Interelectrode length was fixed at 10mm (Fig 2).

1.4. Experiment B: Comparison of ablation performance of conventional electrodes and Octopus MP

Using the single switching mode, RF energy (maximum 200 W) was delivered to one of the two electrodes and was automatically switched between the two electrodes depending on the elevation of the tissue impedance for 6 minutes. Interelectrode length was fixed at 10mm.

1.5. Experiment C: Octopus MP, effect verification experiment of temperature

monitoring RFA

Assuming that there is an organ that should not be thermally damaged at a distance of 10 mm around the target electrode, the temperature sensor effect of the Octopus MP electrode was confirmed. The interelectrode length was fixed at 10mm, the temperature sensor electrode was assumed to be 5mm away from the place assumed to be the surrounding organ, and the output was terminated when it reached 60 degrees during ablation. RF energy was 200 watt, and single switching mode was used.

1.6. Experiment D: Octopus MP, effect verification of injection

After inserting the multipurpose electrode into the center of the two electrodes, chilled normal saline was injected for 3 minutes after ablation for 3 minutes at a rate of 0.5cc/1min (using injection pump). Interelectrode length was fixed at 10mm. RF energy was 200 watt, and single switching mode was used (Fig 3).

1.7. Assessment of the ablation zone

The livers were removed enbloc, and liver segments with ablation zones were excised along the electrode tract, which were subsequently sliced in the transverse plane perpendicular to the electrode tract axis at 5-7 mm intervals such that the sections included the largest areas of the ablation zone. To prevent any bias in the ablation size measurements, slices were photographed beside a ruler on a copy stand using a digital camera (Nikon Coolpix S6900; Nikon Inc., Tokyo, Japan). The ablation volume was calculated using the following formula: $\pi (Dv \times Dmx \times Dmi)/6$.

1.8. In vivo study

This study was approved by our Institutional Animal Care and Use Committee, and all experiments were conducted following institutional guidelines (IACUC No. 20−0222−S1A0[1]).

1.9. Anesthesia and Surgery in Animals

Sixteen male pigs (mean weight, 65 kg; range, 60-70 kg) were used in the in vivo studies. Animals were sedated by intramuscular administration of zolazepam (5 mg/kg, Zoletil; Virbac) and xylazine (10 mg/kg; Rompun, Bayer−Schering Pharma), intubated and ventilated during the experiments. Anesthesia was maintained with 1%-4% isoflurane (IsoFlo1, Abbott Laboratories) inhalation in pure oxygen gas with mechanical ventilation. Before the midline incision, the pigs were placed in the supine position and draped sterile. One of the authors (with three years of experience in RFA experiments) performed the ablation procedures under the guidance of ultrasonography (6-12 MHz linear transducer; Accuvix XQ; Medison). The vital signs of the animals, including the pulse rate, electrocardiogram, and temperature, were carefully monitored during the entire procedure.

1.10. In Vivo Experimental Setting

We performed two in vivo experiments to compare the efficiency and safety of RFA techniques in porcine liver using Octopus MP electrodes. Two ablation zones for saline instillation experiments and four ablation zones for temperature measurement experiments were generated in the liver of each animal. Therefore, 96 ablation zones were created in 16 pigs.

Experiment 1 compared the feasibility and efficiency of saline instillation using the Octopus MP electrode by assessing the ablation zone. In this experiment, the pigs were divided into two groups: the Octopus MP electrode with saline instillation (n = 16) and the conventional electrode group (n = 16). In the Octopus MP electrode group, saline was instilled between the two electrodes, and ablation was performed for 6 minutes each. In both groups, clustered separable electrodes were inserted into the liver parenchyma through a triangular acryl plate containing multiple holes to maintain an interelectrode distance of 2 cm (Fig. 2)

Experiment 2 was conducted to evaluate the safety of the Octopus MP electrode by measuring the temperature. In this experiment, the pigs were divided into two groups: the Octopus MP group (n = 16) and the conventional electrode group (n = 16). In the Octopus MP electrode group, ablation was immediately stopped after the tissue temperature reached 60° C. In the conventional electrode group, ablation was performed for 6 minutes without interruption. As a safety parameter, the presence of thermal injury in adjacent organs or structures, including the gallbladder (GB) and colon was controlled during the procedure. The Octopus MP applicator was inserted into the liver 1 cm away from the GB and colon (Fig. 2). The other two electrodes were inserted through the same acrylic plate used in Experiment 1, thereby ensuring an interelectrode distance of 2 cm and not exceeding 1.5 cm from the liver margin.

1.11. Ablation Protocols

In Experiment 1, RF energy was applied in single switching monopolar mode for 6 minutes. The maximum delivered RF energy was 200 watts. In Experiment 2, the thermal injury was evaluated. The maximum RF energy and ablation times were the same as those used in Experiment 1.

1.12. Assessment of the Ablation Zone

All animals were euthanized by intravenous injection of potassium chloride immediately after the RFAs. The livers were removed en-bloc, and liver segments with ablation zones were excised along the electrode tract and were subsequently sliced in the transverse plane perpendicular to the electrode tract axis at 5-7 mm intervals such that the sections included the largest areas of the ablation zone. To prevent any bias in the ablation size measurements, the slices were photographed beside a ruler on a copy stand using a digital camera (Nikon Coolpix S6900; Nikon Inc.). Two observers (a technician with 3 and 5 years of experience in RFA experiments, respectively) measured the vertical diameter (Dv) in the vertical plane and the long-axis diameter (Dmx) and short-axis diameter (Dmi) of the RF-induced ablation zones at the transverse plane with the maximum area in consensus [19]. The ablation volume was calculated using the following formula: π (Dv x Dmx x Dmi)/6.

1.13. Assessment of Thermal Injury

Thermal injury to the adjacent organs was evaluated as a safety parameter. After sacrificing the animals, GB and colon were resected and fixed in a 40 g/L formaldehyde solution. Specimens were cut into 3-mm thick slices, embedded in paraffin, and stained with hematoxylin and eosin for analysis under a light microscope. The slides were then reviewed to determine the presence and depth of thermal injury.

1.14. Statistical Analysis

For each ablation, the results are presented as mean ± standard deviation (SD). Technical parameters were compared using the t test. The rate of thermal injury was compared using the chi-square test. For all statistical analyses, p values < 0.05 were considered statistically significant using the MedCalc statistical software (version 20.0; MedCalc Software).

Chapter 3. Results

Ex vivo study

1.1. Verification of performance according to varying exposure length (20, 25, 30mm)

When comparing the performance of the Octopus MP electrode and the conventional electrode by length (20, 25, 30mm), there was no statistically significant difference in total energy and ablation volume (P = 0.95, 0.93, respectively) (Table 1) (Fig 5).

1.2. Comparison of ablation performance of conventional electrodes and Octopus MP electrode

To compare the ablation performance of the Octopus MP electrode and the conventional electrode, the electrode length was fixed at 25mm, and 5 experiments were conducted each. There was no statistically significant difference in total energy and ablation volume in ablation performance between the two electrodes (P = 0.93, 0.33, respectively) (Table 2) (Fig 6).

1.3. Octopus MP, effect verification experiment of temperature monitoring RFA

When the temperature reached 60 degrees in the temperature sensing of the Octopus MP electrode, the ablation was terminated and the actual ablation was confirmed. It took an average of 110 seconds for the temperature to reach 60 degrees, and it was confirmed that the actual ablation was only ablated up to an average of 8.9 mm outside the electrode. In the case of the conventional electrode, which was ablated for up to 6 minutes without temperature monitoring, it was confirmed that ablation was performed up to an average of 13.8 mm outward.

In the temperature measurement experiment group, the total energy and ablation volume were statistically significantly lower than the conventional electrode group that did not measure temperature ($P < 0.001$, respectively) (Table 3) (Fig 7).

1.4. Octopus MP, effect verification of injection

The group injected with saline had a statistically significantly lower impedance than the non−injected group, and the total energy and ablation volume were higher ($P<0.001$, respectively) (Table 4) (Fig 8, 9).

In vivo study

1.1. Comparison between the Octopus MP and Conventional Electrode Groups in Experiment 1

We excluded one ablation zone in the Octopus MP electrode group and four ablation zones in the conventional electrode group owing to the perivascular location of the large vessels (> 3 mm). Therefore, 15 and 12 ablation zones in the Octopus MP and conventional electrode groups, respectively, were included. The ablation volume (15.7 ± 4.26 cm^3 vs. 12.5 ± 2.14 cm^3), the Dv of the ablative zone (3.10 ± 0.56 cm vs.2.57 ± 0.27 cm), and the total energy delivered (5.48 ± 0.49 Kcal vs. 5.04 ± 0.49 Kcal) were significantly higher in the Octopus MP electrode group than in the conventional electrode group (p = 0.027, 0.005, 0.029, respectively). The mean electrical impedance of the Octopus MP electrode group was significantly lower than that of the conventional electrode group (74.1 ± 4.01 Ω vs. 80.5 ± 10.0 Ω, $p = 0.047$) (Table 1, Fig. 3).

1.2. Comparison between the Octopus MP Electrode and Conventional Electrode Groups in Experiment 2

In eight procedures in the Octopus MP electrode group and ten in the conventional electrode group, the ablation zones passed through a large vessel. These ablations were excluded from the results because the ablation volume and time to reach 60° C were affected by the heat sink effect. Therefore, 12 ablations for each anatomical location (i.e., either near the GB or the colon) were analyzed in the Octopus MP electrode group, and 11 for each location were analyzed in the conventional electrode group. The total energy delivered around the GB (2.65 ± 1.07 Kcal vs. 5.04 ± 0.66 Kcal) and colon (2.58 ± 0.57 Kcal vs. 5.17 ± 0.90 Kcal) were significantly lower in the Octopus MP electrode group than in the conventional electrode group ($p < 0.001$, 0.001, respectively). There were no significant differences in the ablation volume among the groups (13.1 ± 6.81 cm^3 vs. 16.4 ± 5.98 cm^3, $p = 0.227$; 14.4 ± 4.4 cm^3 vs. 13.7 ± 3.51 cm^3, $p = 0.665$, respectively). The other size parameters, including diameter, were not significantly different between the groups (Table 2). The average time to reach 60° C was 172.7 ± 68 seconds in the ablation around the GB and 165.5 ± 54 seconds around the colon. Thermal injury to the adjacent GB and colon was less frequently noted in the Octopus MP electrode group than in the conventional electrode group (16.7% [2/12] vs. 90.9% [10/11], $p < 0.001$; 8.3% [1/12] vs. 90.9% [10/11], $p < 0.001$) (Table 2, Fig. 4).

Chapter 4. Discussion

Our in vivo study demonstrated that RFA using the Octopus MP electrode is capable of saline instillation and direct tissue temperature measurement, showing better efficiency in creating ablation zones, and a better safety profile than RFA using a conventional internally cooled electrode. The total energy delivered and ablation volume of RFA using the Octopus MP electrodes with saline perfusion were significantly larger than those with the conventional electrode. In contrast, the electrical impedance was significantly lower in the Octopus MP electrode group than that in the conventional electrode group. In addition, in the second set of RF experiments, thermal injury to the adjacent organs was also significantly lower in the octopus MP electrode group with direct tissue temperature measurements than that in the conventional electrode group. To improve the efficiency of achieving an ablation zone for treating liver malignancies while avoiding complications, RF electrodes should ideally allow the following features: 1) complete ablation of the lesion and the surrounding margin, 2) sparing of the neighboring organs from the risk of thermal injury, 3) reduction of the damage of normal tissue, and 4) accomplishment of all the above features through one session of percutaneous insertion [20]. Based on our study results, we believe that RFA using Octopus MP electrodes may contribute to producing ablation zones conformable to the index tumor and safety margin while decreasing unnecessary thermal damage to adjacent vital structures.

A total of 4 experiments were conducted in the ex vivo study. In the first and second experiments, since the Octopus MP electrode is a variable-length electrode, it was necessary to compare the ablation performance with the conventional electrode according to each length (20mm, 25mm, 30mm), and the experimental results showed no statistically significant difference with the conventional electrode in the ablation performance. This means that when performing RFA, even if the length is varied according to the size of the tumor or to form the desired ablation zone, it shows the same performance as the conventional electrode of the same length. Also, this can be said to be meaningful in that it broadened the range of choices with one electrode.

The third experiment was an experiment to verify the effect using a temperature monitoring electrode. Tumors often occur near peripheral organs such as GB or colon, injury due to RFA can occur. When organ damage occurs, the patient's hospitalization period becomes longer and the possibility of mortality increases, so RFA is carefully performed, but the problem is that there is no way to confirm damage. However, if the temperature monitoring electrode is used, safe ablation becomes possible because it can be checked whether or not the tissue reaches 60 degrees where it is damaged.

The fourth experiment was an experiment comparing energy delivery and ablation volume through saline injection. Even if RFA is performed for HCC larger than 3 cm, a large ablation zone must be created, which increases the procedure time and increases the possibility of local tumor progression. In addition, the impedance increases during ablation, impairing ablation performance. If the ablation range can be widened while effectively lowering impedance, the energy delivery can be improved and the ablation volume can also be made larger. As saline injection was injected in this experiment, the impedance was statistically significantly lower than that of the conventional electrode, and as a result, the total energy delivery and ablation volume were significantly increased than that of the conventional electrode.

In the first experiment, the mean ablation volume of RFA using the Octopus MP electrodes with saline perfusion was significantly larger than that using the conventional electrode. Several studies have demonstrated that LTP is significantly lowered if a safety margin of > 5 mm around the index tumor is achieved [21,22]; therefore, a large ablation zone is indispensable in RFA [23]. In our study, the RF energy was significantly higher in the Octopus MP electrode group with saline perfusion than in the conventional electrode group, while the electrical impedance was significantly lower. In the case of the conventional Octopus electrode, a larger ablation zone can be created by switching to monopolar mode compared to consecutive overlapping ablations [24]. However, because the high−frequency current is concentrated within 5 mm of the tissue around the electrodes, increased charring and high impedance may occur, resulting in inefficient RF energy delivery [9]. Therefore, if the efficiency of the energy delivered is increased by lowering the impedance with saline perfusion, a larger ablation zone can be created and achieve low LTP [25,26]. In our results, when saline instillation was performed through the Octopus MP electrode, the impedance was significantly lower than that of the conventional electrode, which increased the total energy delivered, making it possible to create a large ablation zone.

In the second experiment, we tested the value of direct tissue temperature monitoring during RFA using Octopus MP electrodes by inserting a temperature−sensing applicator around critical organs, such as the GB or colon. The injury to the adjacent GB and colon was less frequently noted in the Octopus MP electrode group than in the conventional electrode group (16.7% [2/12] vs. 90.9% [10/11], 8.3% [1/12] vs. 90.9% [10/11], $p < 0.001$ for all). In the experimental setting, the tissue temperature near the critical organs was measured in real−time using one of the Octopus MP electrodes. and RF energy application was terminated when tissue temperature around the adjacent critical organs was over 60° C. We selected 60° C as the cutoff value because, tumor cells suffer necrosis when a temperature of 60° C or higher is reached and the effect of RFA can be maximized [9,12]; however, if thermal injury occurs in an adjacent organ, there is a higher probability of complication. In this respect, when the ablation zone of the Octopus MP group with temperature sensing was compared with that of the group that underwent RFA for 6 minutes without temperature sensing, no statistically significant difference was observed in ablation volume. Therefore, a higher level of safety could be ensured using the Octopus MP electrodes.

Other potential advantages of the Octopus MP electrodes should be considered. First, as there are two electrodes with adjustable active tip lengths the system can be used for no-touch ablation. Several recent studies have demonstrated better local tumor control of liver malignancies with this approach than conventional tumor puncture techniques, either through percutaneous or laparoscopic approaches [27-29]. Second, since the active tips of the two electrodes are adjustable from 1 cm to 3 cm with a 5 mm step variable, Octopus MP electrodes could be useful in treating asymmetric and ovoid-shaped tumors, especially those with variable diameters that require active tips of different lengths. In addition, these electrodes can be used for the ablation of multiple tumors of different sizes by adjusting the length of the exposed active tip [11]. Finally, Octopus MP electrodes can be used to avoid damage to the adjacent organs by creating a non-spherical ablation volume using different lengths of the active tips [30]. In addition, it is very important to deliver a sufficient amount of high-frequency energy to the tumor to be treated during RFA and to form a sufficient safety margin around the tumor to reduce the recurrence rate. During RFA, the presence or absence of a safety margin is evaluated by looking at the range of high-echo bubble generation on the ultrasound image, but most of them tend to be exaggerated and are inaccurate, and the most accurate method is to directly measure the temperature of the surrounding tissue. However, since most commercially available electrodes can measure temperature at the tip of the electrode, only the temperature of the tissue in direct contact with the electrode needle can be measured, so the temperature of the tissue around the actual tumor cannot be measured. There are drawbacks that are difficult to evaluate. Octopus MP electrode overcomes these disadvantages and enables temperature measurement, enabling detailed cauterization. Fourth, the Octopus MP electrode has micro-hole for saline injection. During ablation, the impedance increases due to the charring effect and the ablation performance decreases. To effectively overcome this, saline injection reduces the impedance to improve energy delivery and increase the ablation volume. In addition, when saline injection as well as therapeutic drugs are injected through this micro−hole, the effect of tumor necrosis can be increased, and a high level of synergy can be expected with the combination of ablation and drug treatment. This is thought to be the significance of this Octopus MP electrode.

This study has several limitations. First, the feasibility and safety of the Octopus MP electrode were evaluated intraoperatively; therefore, we were unable to assess percutaneous RFA. Thus, the feasibility of using an Octopus MP electrode in percutaneous RFA should be evaluated. Second, this study tested a single−energy mode; thus, the results of the current study should be interpreted with caution. Third, this in vivo study was conducted using a relatively small number of animals. However, in this experiment, the effects of saline instillation and temperature measurements of the Octopus MP electrodes were confirmed. Fourth, we only tested the Octopus MP electrode with a single inter−electrode interval of 2 cm. Additional studies using larger inter−electrode intervals are warranted. Finally, RF ablation was not performed using a tumor mimicker. This prevented the evaluation of safety margins and technical success. However, because tumor mimickers possess different properties from the tissue texture of target tumors, their application in clinical practice is challenging.

Chapter 5. Conclusion

Our results demonstrated that the Octopus MP electrodes, which are capable of saline instillation and temperature measurement, induced lower electrical impedance, enabling a larger ablation volume and total energy delivery. Moreover, it demonstrated the potential to provide a better safety profile with less thermal injury to adjacent organs compared to conventional electrodes.

Tables and Figures

Table 1. *Ex vivo* experiment A

Electrode	Electrode Spec (length, mm)	Impedance (Ω)	Energy (Kcal)	Dmx	Dmi	Dv	Volume
Octopus MP	20	105	3.99	2.49	2.43	3.15	10.01
	25	96	5.18	3.12	2.95	3.65	17.62
	30	91	11.44	3.85	3.77	4.43	33.61
Conventional	20	117	3.72	2.49	2.44	3.43	10.90
	25	98	5.15	3.17	2.73	3.67	16.60
	30	89	11.10	3.8	3.54	4.43	31.16

MP = multi-purpose, Dmx = maximal diameter of the ablative zone, Dmi = minimum diameter of the ablative zone, Dv = vertical diameter of the ablative zone

Table 2. *Ex vivo* experiment B

Electrode	Electrode Spec (length, mm)	No	Impedance (Ω)	Energy (Kcal)	Dmx	Dmi	Dv	Volume
Octopus MP	25	1	85	4.79	3.83	3.18	3.91	24.92
		2	85	5.03	3.62	3.08	3.6	21.00
		3	79	4.47	3.34	3.15	3.62	19.91
		4	88	6.01	3.67	3.31	4.03	25.55
		5	80	6.14	3.73	3.49	3.85	26.25
		Av	83	5.29	3.64	3.24	3.8	23.53
Conventional	25	1	86	5.94	3.7	3.21	3.89	24.17
		2	84	4.68	3.6	3.2	3.65	21.98
		3	88	6.39	3.55	3.15	3.92	22.89
		4	77	4.37	3.24	2.97	3.54	17.81
		5	75	4.84	3.6	3.07	3.84	22.23
		Av	82	5.24	3.54	3.12	3.77	21.82

MP = multi-purpose, Dmx = maximal diameter of the ablative zone, Dmi = minimum diameter of the ablative zone, Dv = vertical diameter of the ablative zone, Av = average

Table 3. *Ex vivo* experiment C

Electrode	Electrode Spec (length, mm)	Temperature	No	Impedance (Ω)	Energy (Kcal)	Dmx	Dmi	Dv	Volume	Time (sec)
Octopus MP	25		1	92	2.62	2.56	2.00	3.27	8.77	112
			2	83	2.39	2.53	1.97	3.27	8.56	101
		60	3	84	2.98	2.73	2.27	3.27	10.60	133
			4	75	2.62	2.67	2.30	3.34	10.75	120
			5	79	2.04	2.59	1.89	3.12	8.02	82
			Av	83	2.53	2.62	2.09	3.25	9.34	110
Conventional	25		1	85	2.19	3.83	3.18	3.91	24.92	
			2	85	2.39	3.62	3.08	3.60	21.00	
			3	79	1.77	3.34	3.15	3.62	19.91	
			4	88	2.87	3.67	3.31	4.03	25.55	
			5	80	3.1	3.73	3.49	3.85	26.25	
			Av	83	2.46	3.64	3.24	3.80	23.53	

MP = multi-purpose, Dmx = maximal diameter of the ablative zone, Dmi = minimum diameter of the ablative zone, Dv = vertical diameter of the ablative zone, Av = average

Table 4. *Ex vivo* experiment D

Electrode	Electrode Spec (length, mm)	Injection	No	Impedance (Ω)	Energy (Kcal)	Dmx	Dmi	Dv	Volume
Octopus MP	25	3min~	1	76	8.03	3.77	3.68	4.03	29.21
			2	74	7.41	3.66	3.52	3.73	25.12
			3	73	7.82	3.83	3.58	3.85	27.62
			4	79	8.21	3.87	3.54	3.92	28.13
			5	76	6.29	3.75	3.61	3.86	27.34
			6	66	7.37	4.13	3.65	3.94	31.08
			7	67	6.81	4.24	3.61	3.93	31.53
			8	66	6.14	3.92	3.52	3.91	28.21
			9	66	8.02	4.03	3.51	4.00	29.56
			10	65	6.76	3.91	3.77	3.87	29.83
			Av	71	7.29	3.91	3.60	3.90	28.76
Conventional	25		1	85	4.79	3.83	3.18	3.91	24.92
			2	85	5.03	3.62	3.08	3.60	21.00
			3	79	4.47	3.34	3.15	3.34	19.91
			4	88	6.01	3.67	3.31	3.53	25.55
			5	80	6.14	3.73	3.49	3.59	26.25
			Av	83	5.29	3.64	3.24	3.48	23.53

MP = multi-purpose, Dmx = maximal diameter of the ablative zone, Dmi = minimum diameter of the ablative zone, Dv = vertical diameter of the ablative zone, Av = average

Table 5. Comparison of measured values of technical parameters between Octopus MP electrode with saline instillation and conventional electrode

Parameters	Octopus MP electrode (N = 15)	Conventional electrode (N = 12)	P-value
Total energy delivered (Kcal)	5.48 ± 0.49	5.04 ± 0.49	0.029
Impedance (Ohm)	74.1 ± 4.01	80.5 ± 10.0	0.047
Dmx (cm)	3.97 ± 0.48	3.68 ± 0.37	0.109
Dmi (cm)	2.41 ± 0.33	2.53 ± 0.18	0.282
Dv (cm)	3.10 ± 0.56	2.57 ± 0.27	0.005
Ablation volume (cm^3)	15.7 ± 4.26	12.5 ± 2.14	0.027

MP = multi-purpose, Dmx = maximal diameter of the ablative zone, Dmi = minimum diameter of the ablative zone, Dv = vertical diameter of the ablative zone

Table 6. Comparison of measured values of technical parameters between Octopus MP electrode with saline instillation and conventional electrode

Parameters	Octopus MP electrode (N = 15)	Conventional electrode (N = 12)	P-value
Total energy delivered (Kcal)	5.48 ± 0.49	5.04 ± 0.49	0.029
Impedance (Ohm)	74.1 ± 4.01	80.5 ± 10.0	0.047
Dmx (cm)	3.97 ± 0.48	3.68 ± 0.37	0.109
Dmi (cm)	2.41 ± 0.33	2.53 ± 0.18	0.282
Dv (cm)	3.10 ± 0.56	2.57 ± 0.27	0.005
Ablation volume (cm^3)	15.7 ± 4.26	12.5 ± 2.14	0.027

MP = multi-purpose, Dmx = maximal diameter of the ablative zone, Dmi = minimum diameter of the ablative zone, Dv = vertical diameter of the ablative zone

Table 7. Comparison of measured values of technical parameters between Octopus MP electrode with temperature measurement and conventional electrode.

Parameters	Adjacent organ	Octopus MP electrode (N = 12)	Conventional electrode (N = 11)	P-value
	GB			
Total energy delivered (Kcal)		2.65 ± 1.07	5.04 ± 0.66	<0.001
Impedance (Ohm)		78 ± 8.74	74.2 ± 7.86	0.296
Dmx (cm)		3.68 ± 0.66	3.97 ± 0.29	0.180
Dmi (cm)		2.31 ± 0.55	2.44 ± 0.47	0.580
Dv (cm)		2.81 ± 0.52	3.16 ± 0.59	0.142
Ablation volume (cm^3)		13.1 ± 6.81	16.4 ± 5.98	0.227
Time to reach 60℃ (sec)		172.7 ± 68		
Thermal injury		2 (16.7 %)	10 (90.9 %)	<0.001
	Colon			
Total energy delivered (Kcal)		2.58 ± 0.57	5.17 ± 0.90	<0.001
Impedance (Ohm)		84 ± 10.8	82.3 ± 8.15	0.661
Dmx (cm)		3.93 ± 0.36	3.85 ± 0.36	0.585
Dmi (cm)		2.31 ± 0.49	2.26 ± 0.29	0.36
Dv (cm)		2.96 ± 0.38	2.96 ± 0.39	0.987
Ablation volume (cm^3)		14.4 ± 4.4	13.7 ± 3.51	0.665
Time to reach 60℃ (sec)		165.5 ± 54		
Thermal injury		1 (8.3 %)	10 (90.9 %)	<0.001

MP = multipurpose, Dmx = maximal diameter of the ablative zone, Dmi = minimum diameter of the ablative zone, Dv = vertical diameter of the ablative zone, GB = gallbladder.

Fig. 1. Prototype Octopus multipurpose electrodes (A) and diagram of the thin applicator (B).

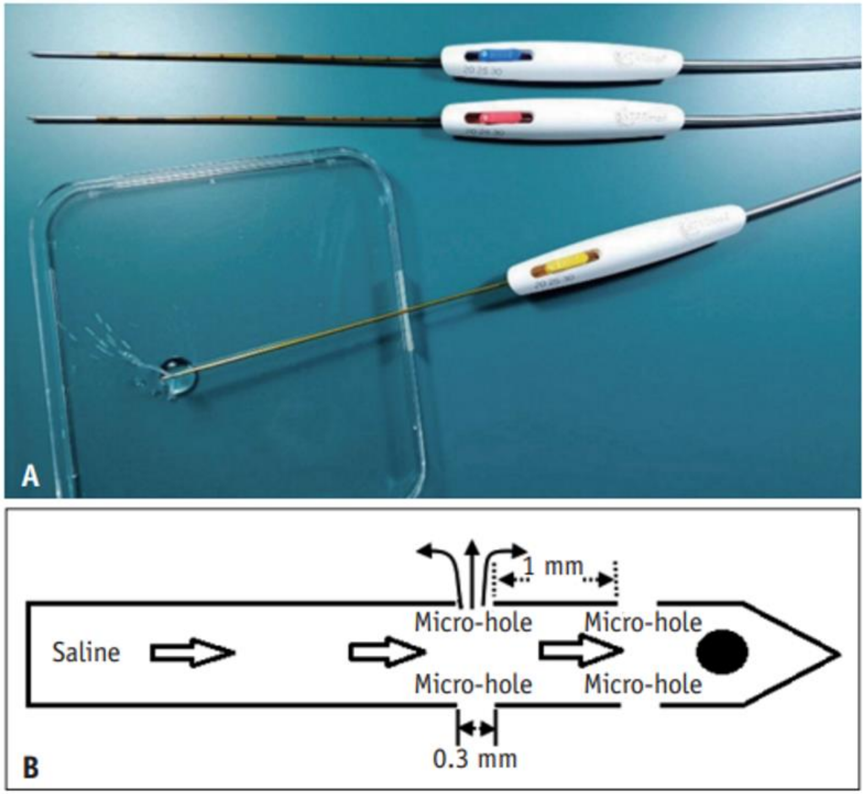


Fig. 2. *Ex vivo* experiment A

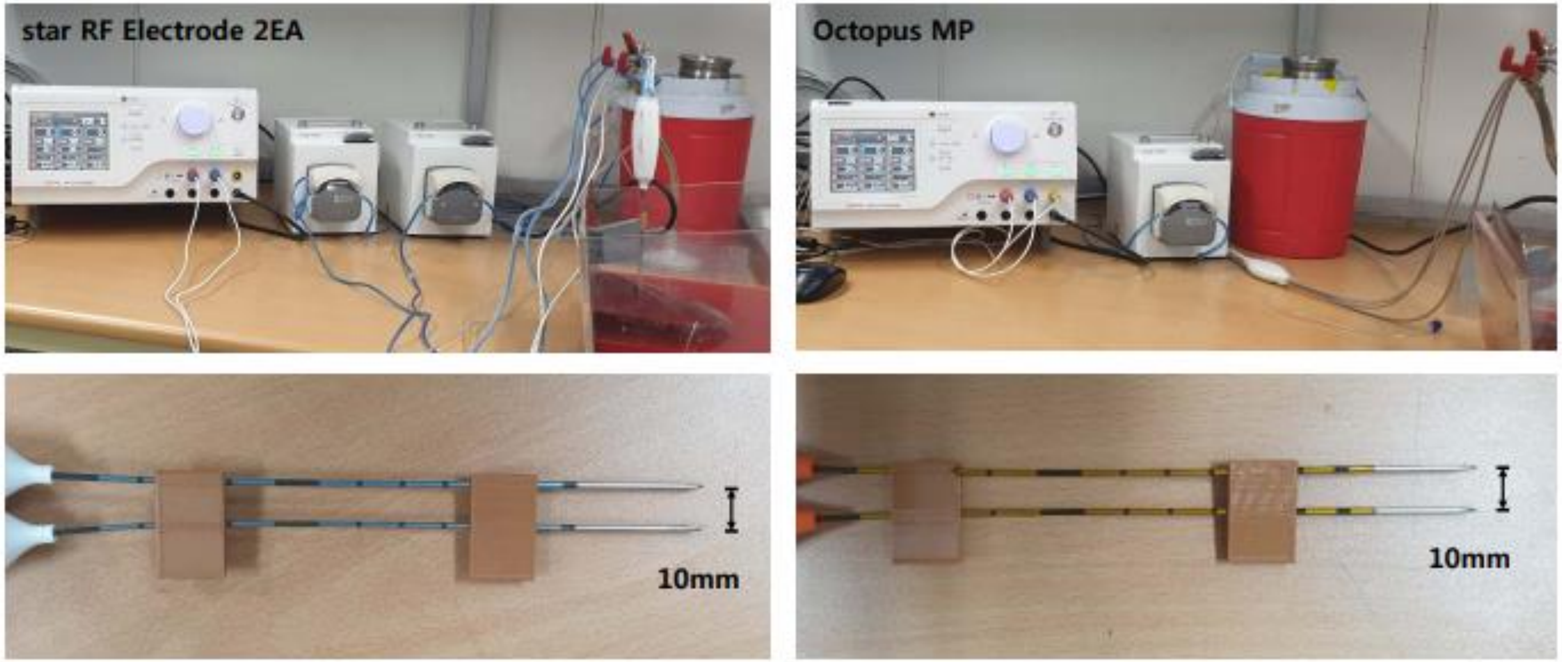


Fig. 3. *Ex vivo* experiment D

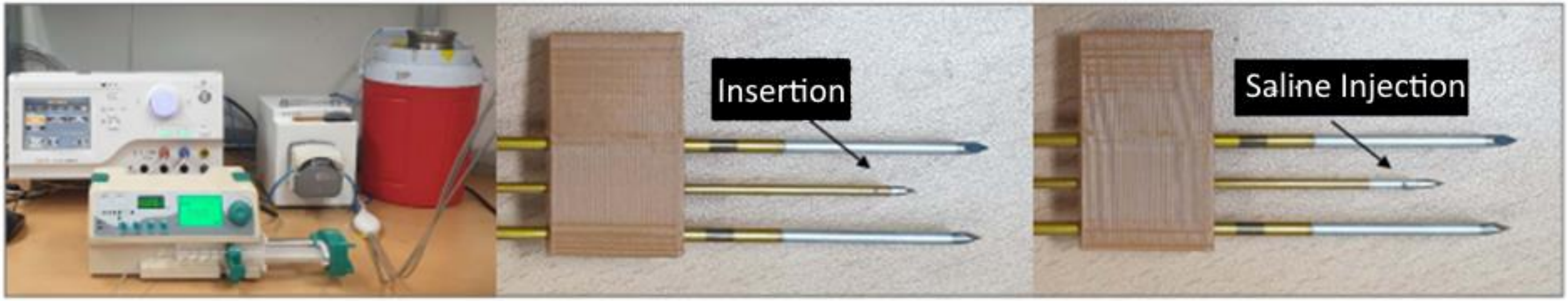


Fig. 4. Diagram for electrode positions for experiments 1 (A) and 2 (B). Black circle: saline instillation/temperature measurement electrode. Cross circle: active ablation electrode

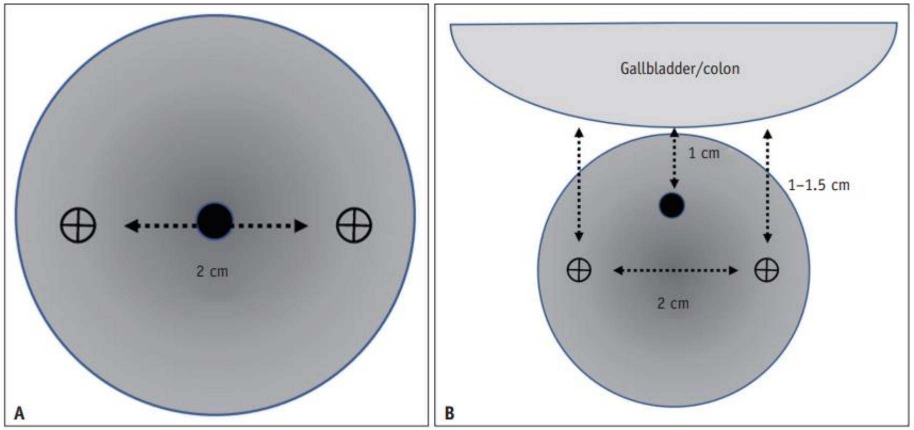


Fig. 5. Photograph of e*x vivo* experiment A

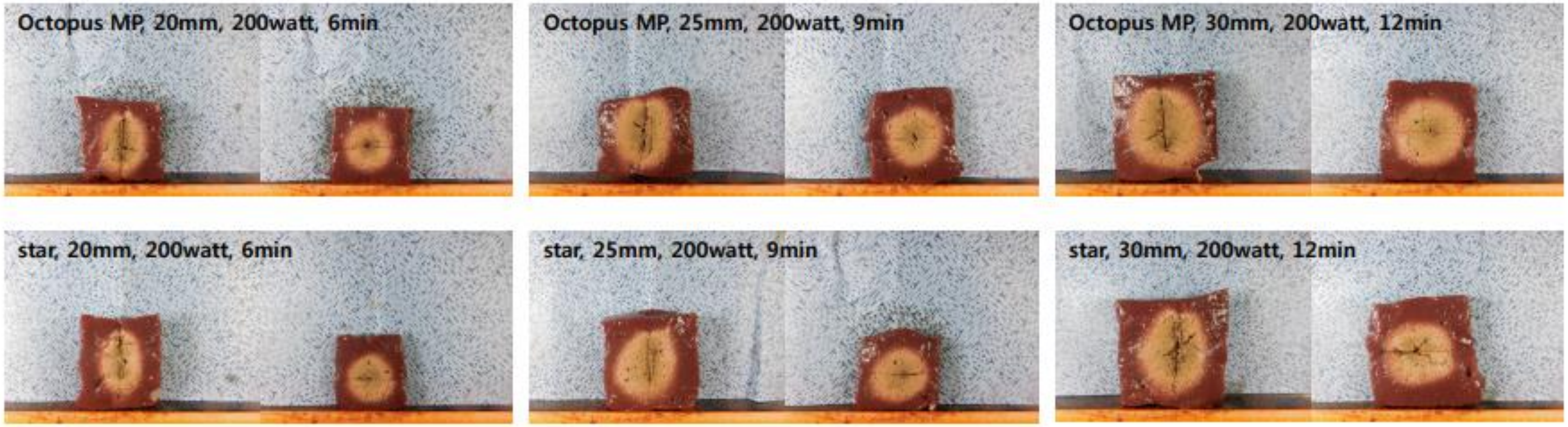
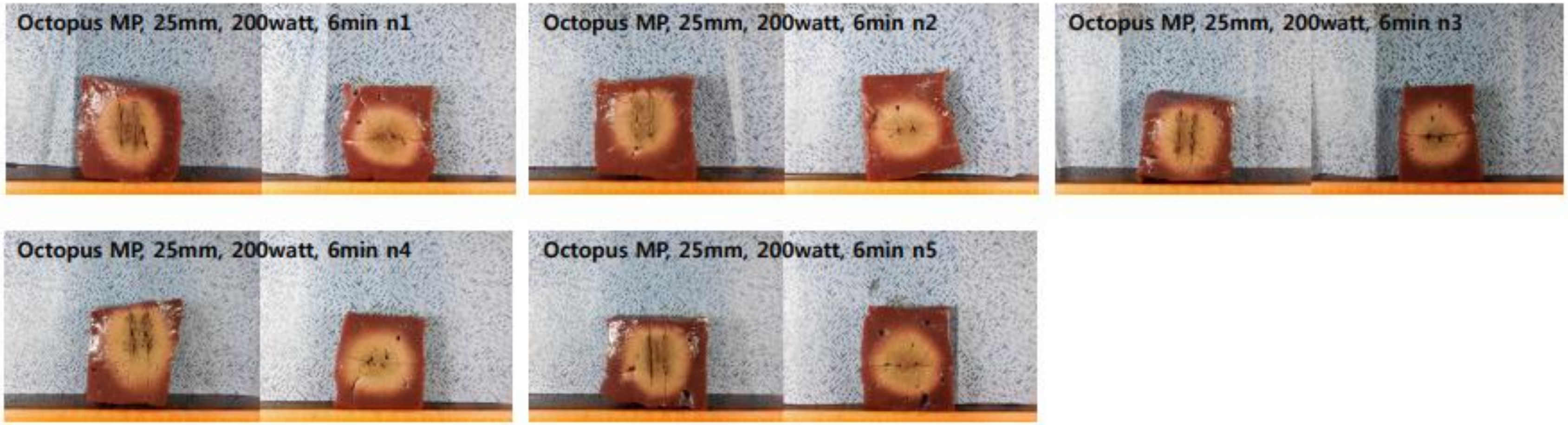
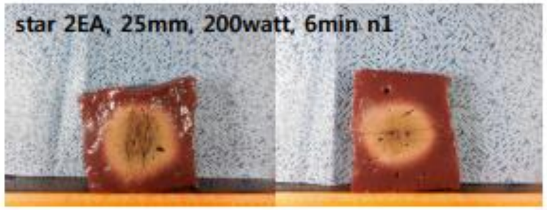
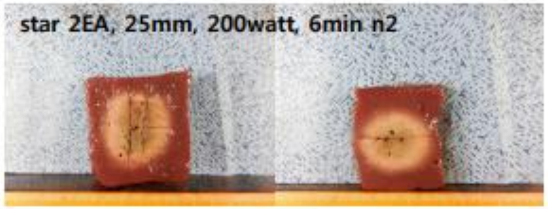


Fig. 6. Photograph of e*x vivo* experiment B




star 2EA, 25mm, 200watt, 6min n1

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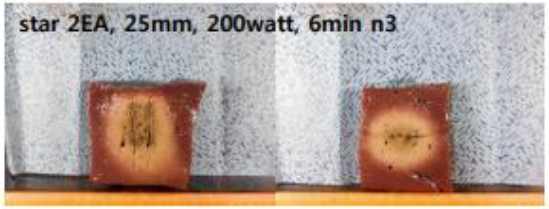
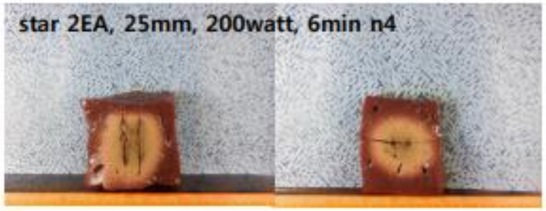
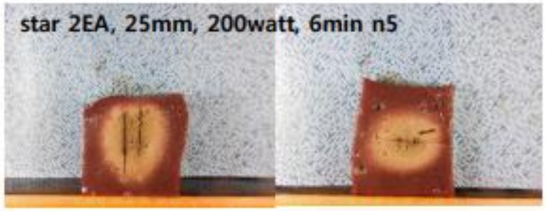

star 2EA, 25mm, 200watt, 6min n3

star 2EA, 25mm, 200watt, 6min n4

star 2EA, 25mm, 200watt, 6min n5

Fig. 7. Photograph of e*x vivo* experiment C

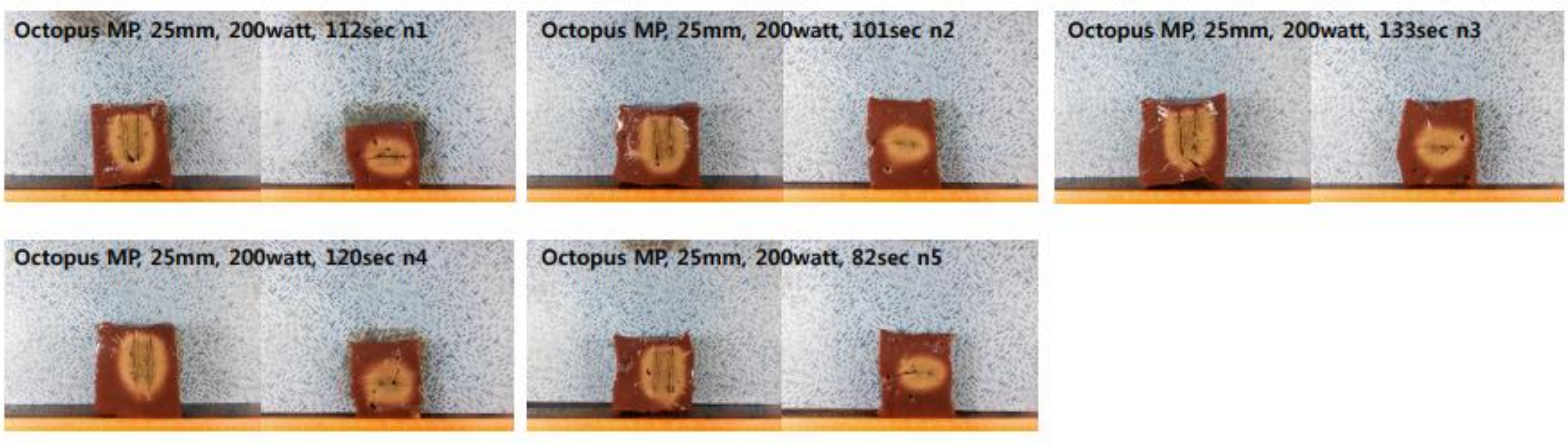
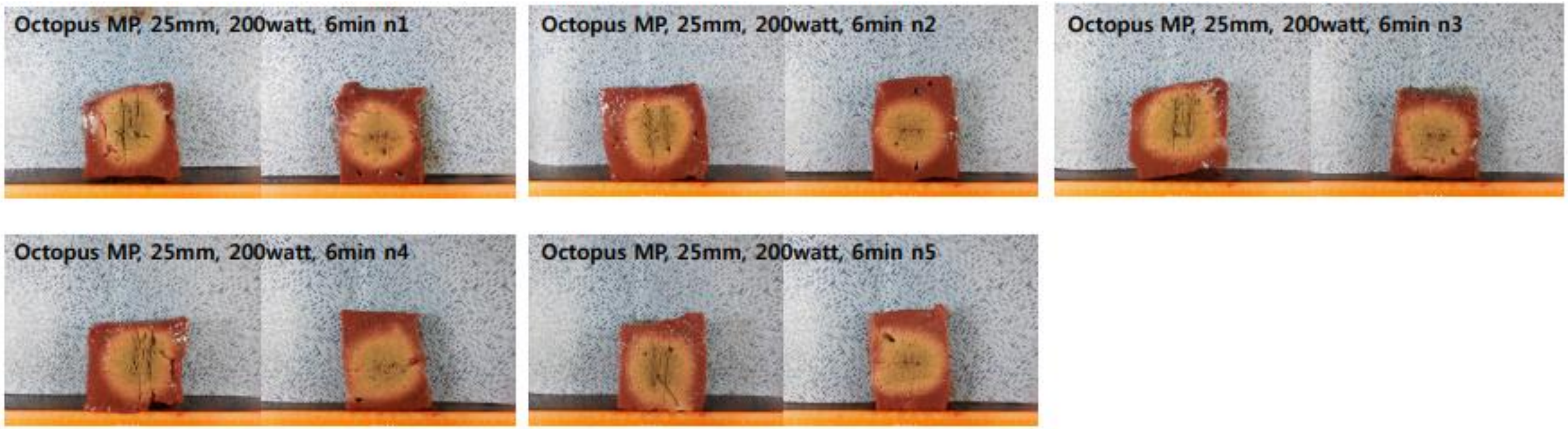
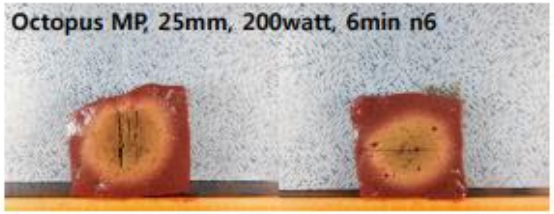
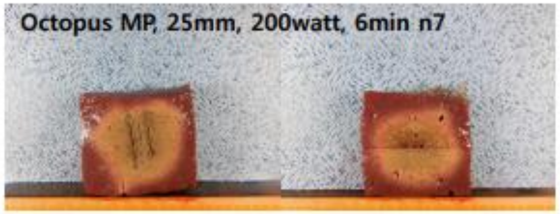
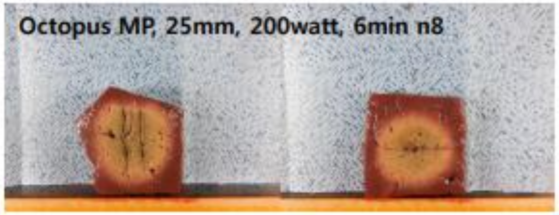


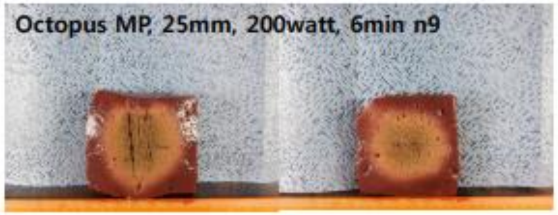
Fig. 8. Photograph of e*x vivo* experiment D




Octopus MP, 25mm, 200watt, 6min n6


Octopus MP, 25mm, 200watt, 6min n7


Octopus MP, 25mm, 200watt, 6min n8


Octopus MP, 25mm, 200watt, 6min n9

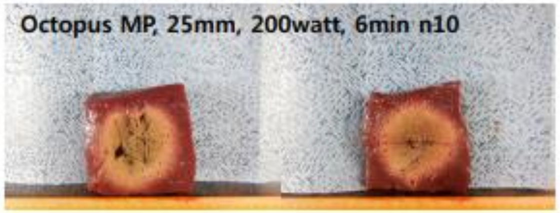

Octopus MP, 25mm, 200watt, 6min n10

Fig. 9. Photograph of e*x vivo* experiment D

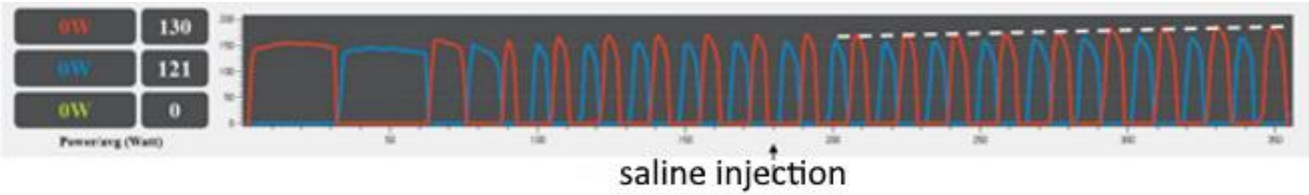


Fig.10. Photographs showing transverse planes of the specimen for experiments 1.
A, B. Saline instillation, ablation volume = 18.8 cm^3. **C, D.** Without saline instillation, ablation volume = 11.4 cm^3.

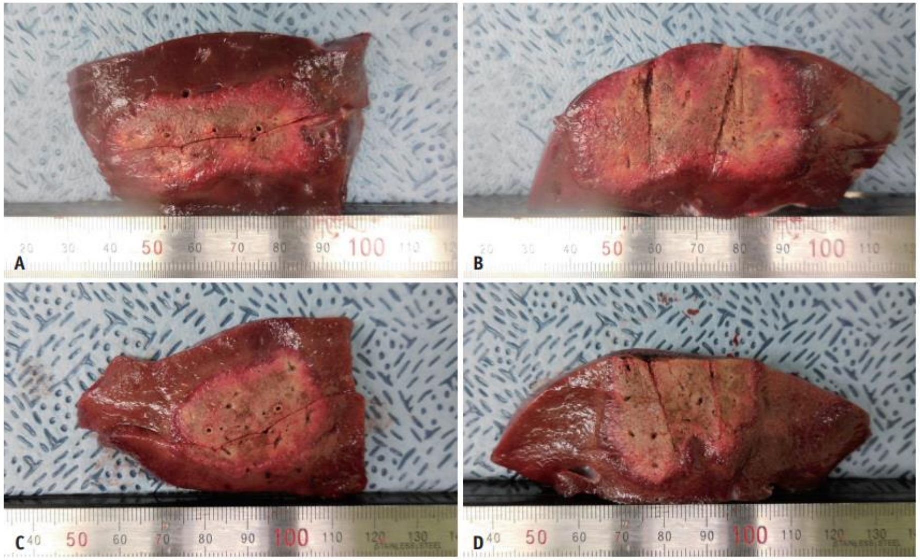
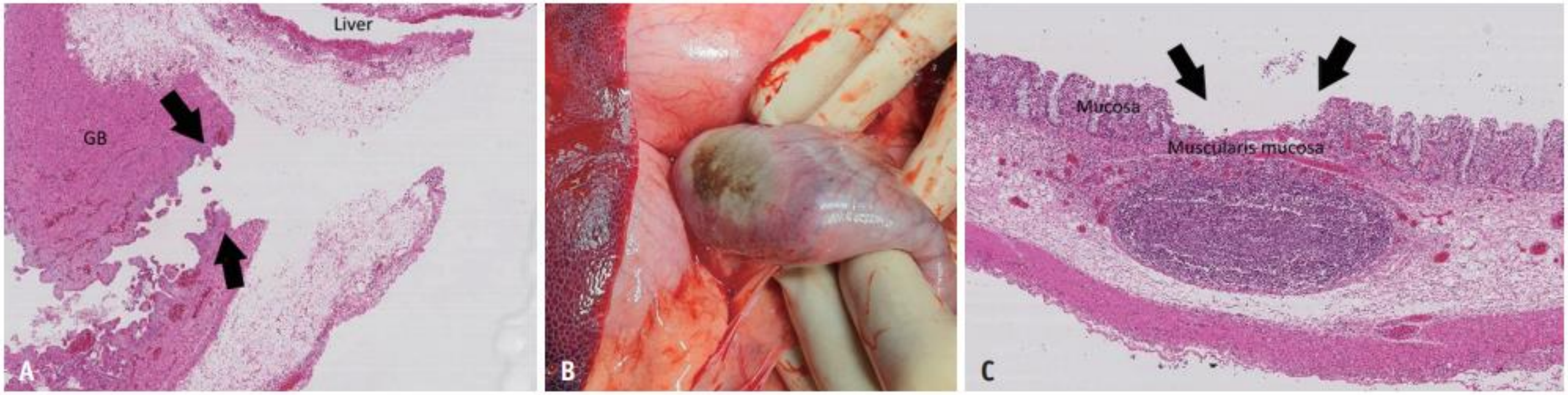


Fig.11. In the conventional electrode group, gallbladder specimen and adjacent liver parenchyma with hematoxylin and eosin staining (H&E) show thermal injury to the mucosa. Perforation is occurred (a). Colon gross specimen (b) shows thermal injury to mucosa. Mucosal ulceration and injury to muscularis mucosa are present (c) (x100).



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Ⅳ. Perfused hypertonic saline-augmented needle enlarges ablation zones in ex vivo

Abstract

목표: 생체 내 돼지 간에서 식염수 점적 및 직접 조직 온도 측정이 가능한 Octopus 다목적(MP) 전극과 고주파 절제(RFA)용 기존 전극을 비교합니다.

재료 및 방법: 생체 외 연구에서 총 4개의 실험이 수행되었습니다. 실험 A와 B는 기존 전극과의 절제 성능을 비교하였으며, 노출 길이 변화(20mm, 25mm, 30mm)에 따른 성능을 비교하였다. 실험 C에서는 온도감지전극의 효과를 검증하였다. 절제 중 온도가 60도에 도달하면 출력을 종료하고, 대상 전극 주변 10mm 거리에 열손상을 주면 안 되는 장기가 있다고 가정했다. 실험 D는 식염수 주입에 따른 성능 차이를 실험하였다. 두 개의 전극 중앙에 다목적 전극을 삽입하고 절제 후 3분부터 3분간 식염수를 주입하여 성능을 비교하였다. 생체 내 연구에서는 16마리의 돼지를 사용하였다. 첫 번째 실험에서는 Octopus MP 전극(n = 15 절제 영역)과 기존 전극(n = 12 절제 영역)을 사용하여 간에서 6분 동안 RFA를 수행하여 식염수 주입의 효과를 조사했습니다. 두 전극의 절제 에너지, 전기 임피던스 및 절제 부피를 비교했습니다. 두 번째 실험에서는 직접 조직 온도 모니터링 및 기존 전극(각각에 대해 n = 11개 절제 영역)이 있는 Octopus MP 전극(각각에 대해 n = 12개 절제 영역)을 사용하여 담낭(GB) 및 결장 근처에서 RFA를 수행했습니다. Octopus MP 전극군에서는 온도가 60˚ C 이상으로 상승하면 RFA를 중단한 반면, 기존 전극군에서는 총 6분 동안 RFA를 수행하였다. 열 손상은 병리학적 검사에 의해 두 그룹 사이에서 평가 및 비교되었습니다.

결과: 생체 외 연구에서 기존 전극과 Octopus MP 전극을 비교했을 때, 실험 A와 B에서 노출 길이에 따른 변화와 성능 측면에서 두 전극 사이에 통계적으로 유의한 차이는 없었다. 온도 측정에서 총 에너지와 절제 부피는 온도를 측정하지 않은 기존 전극 그룹보다 통계적으로 유의하게 낮았다(각각 $P<0.001$). 식염수를 주입한 그룹은 주입하지 않은 그룹보다 임피던스가 통계적으로 유의하게

낮았고 총 에너지와 절제 부피는 실험 D에서 더 높았다(각각 P<0.001). 생체 외 실험에서 첫 번째 실험에서 Octopus MP 전극 그룹에서 전달된 절제 부피와 총 에너지는 기존 전극 그룹(15.7 ± 4.26 cm^3 vs. 12.5 ± 2.14 cm^3, p = 0.027; 5.48 ± 0.49 Kcal vs. 5.04 ± 0.49 Kcal, p = 0.029)보다 훨씬 컸습니다. 두 번째 실험에서 GB 및 결장에 대한 열 손상은 기존 전극 그룹보다 Octopus MP 전극 그룹에서 덜 자주 나타났습니다(16.7% [2/12] vs. 90.9% [10/11] GB 및 8.3 결장의 경우 % [1/12] 대 90.9% [10/11], 모두 p <0.001). GB(2.65 ± 1.07 Kcal vs. 5.04 ± 0.66 Kcal) 및 결장(2.58 ± 0.57 Kcal vs. 5.17 ± 0.90 Kcal) 주변에 전달된 총 에너지는 Octopus MP 전극 그룹에서 기존 전극 그룹보다 현저히 낮았습니다(모두에 대해 p <0.001).

결론: Octopus MP 전극을 사용하는 RFA는 기존 전극에 비해 더 큰 절제 부피를 유도하고 인접 장기에 대한 열 손상이 적었습니다.