การศึกษาเปรียบเทียบระหว่างวิธีการสวิตซ์แบบหลายขั้วและวิธีการสวิตซ์แบบสองขั้ว ในการจี้เนื้อตับด้วยคลื่นความถี่วิทยุที่ใช้หลายอิเล็กโทรดร่วมกับการเปลี่ยนตำแหน่งของอิเล็กโทรด

นางสาวจุฑามาศ พูผุด

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาวิทยาศาสตร์การแพทย์
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ปีการศึกษา 2550
ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

COMPARISON BETWEEN SWITCHING MULTIPOLAR AND SWITCHING BIPOLAR METHODS HEPATIC RADIOFREQUENCY ABLATION USING MULTIPLE ELECTRODES WITH ELECTRODE REPLACEMENTS

Miss Jutamart Pupud

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

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Thesis Title COMPARISON BETWEEN SWITCHING MULTIPOLAR AND SWITCHING BIPOLAR METHODS HEPATIC RADIOFREQUENCY ABLATION USING MULTIPLE ELECTRODES WITH ELECTRODE REPLACEMENTS
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จุฑามาศ พูผุด : การศึกษาเปรียบเทียบระหว่างวิธีการสวิตซ์แบบหลายขั้วและวิธีการสวิตซ์แบบสองขั้วในการจี้เนื้อตับด้วยคลื่นความถี่วิทยุที่ใช้หลายอิเล็กโทรดร่วมกับการเปลี่ยนตำแหน่งของอิเล็กโทรด. (COMPARISON BETWEEN SWITCHING MULTIPOLAR AND SWITCHING BIPOLAR METHODS HEPATIC RADIOFREQUENCY ABLATION USING MULTIPLE ELECTRODES WITH ELECTRODE REPLACEMENTS) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: รศ.นพ.ธันวา ตันสถิตย์, 66 หน้า.

วัตถุประสงค์ เพื่อเปรียบเทียบประสิทธิภาพของวิธีการจี้เนื้อตับด้วยคลื่นความถี่วิทยุที่ใช้หลายอิเล็กโทรดร่วมกับการเปลี่ยนตำแหน่งของอิเล็กโทรด ระหว่างวิธีการสวิตซ์แบบหลายขั้วและวิธีการสวิตซ์แบบสองขั้วในการจี้เนื้อตับของสุกรนอกร่างกายสัตว์ทดลอง

วิธีการศึกษา ใช้เครื่องผลิตคลื่นความถี่วิทยุและอิเล็กโทรด 3 อันทำการจี้เนื้อตับของสุกรจำนวน 50 บริเวณ โดยวิธีการสวิตซ์แบบหลายขั้วจำนวน 25 บริเวณและวิธีการสวิตซ์แบบสองขั้วจำนวน 25 บริเวณ แต่ละบริเวณที่ทำการจี้ด้วยทั้งสองวิธีจะได้รับพลังงานคลื่นความถี่วิทยุผ่านทางอิเล็กโทรดทั้งหมดสามรอบเป็นเวลา 12 นาที, 10 นาทีและ 8 นาที ตามลำดับ ดังนั้นเวลารวมของแต่ละบริเวณคือ 30 นาที ค่าระยะห่างระหว่างอิเล็กโทรดของแต่ละรอบคือ 4, 5.5 และ 7 เซนติเมตร ตามลำดับ จากนั้นบันทึกค่ากระแสไฟฟ้า, กำลังไฟฟ้า, ศักย์ไฟฟ้า และอุณหภูมิของเนื้อตับที่เปลี่ยนแปลงไปทุกๆ 1 นาที จากนั้นนำเนื้อตับมาตัดเพื่อวัดค่าเส้นผ่านศูนย์กลางในแนวขวางที่มากที่สุดและที่น้อยที่สุด และค่าเส้นผ่านศูนย์กลางในแนวตั้ง นำค่าเส้นผ่านศูนย์กลางมาคำนวณหาปริมาตรและอัตราส่วนของรูปร่างของแต่ละบริเวณ จากนั้นทำการเปรียบเทียบค่าทั้งหมดของทั้งสองวิธี

ผลการศึกษา ค่าเฉลี่ยของอุณหภูมิสุดท้ายในเนื้อตับของวิธีการสวิตซ์แบบหลายขั้วและวิธีการสวิตซ์แบบสองขั้วคือ 74.92 ± 7.41 องศาเซลเซียส และ 70.92 ± 8.82 องศาเซลเซียส ตามลำดับ ($p = 0.089$) วิธีการสวิตซ์แบบหลายขั้วทำให้เกิดปริมาตรของเนื้อตับที่ถูกจี้มากกว่าวิธีการสวิตซ์แบบสองขั้ว (156.51 ± 26.81 ลูกบาศก์เซนติเมตร และ 125.49 ± 29.72 ลูกบาศก์เซนติเมตร ตามลำดับ, $p < 0.000$)

สรุปผล ในการจี้เนื้อตับด้วยคลื่นความถี่วิทยุที่ใช้หลายอิเล็กโทรดร่วมกับการเปลี่ยนตำแหน่งของอิเล็กโทรด วิธีการสวิตซ์แบบหลายขั้วมีประสิทธิภาพดีกว่าวิธีการสวิตซ์แบบสองขั้วในการทำให้เกิดบริเวณเนื้อตับที่ถูกจี้ขนาดใหญ่นอกร่างกายสัตว์ทดลอง

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

สาขาวิชา วิทยาศาสตร์การแพทย์ ลายมือชื่อนิสิต......จุฑามาศ พูผุด......

ปีการศึกษา 2550 ลายมือชื่ออาจารย์ที่ปรึกษาวิทยานิพนธ์หลัก............

497 47123 30: MAJOR MEDICAL SCIENCE
KEY WORDS: RADIOFREQUENCY ABLATION/ SWITCHING MULTIPOLAR MODE/ SWITCHING BIPOLAR MODE

JUTAMART PUPUD: COMPARISON BETWEEN SWITCHING MULTIPOLAR AND SWITCHING BIPOLAR METHODS HEPATIC RADIOFREQUENCY ABLATION USING MULTIPLE ELECTRODES WITH ELECTRODE REPLACEMENTS. THESIS PRINCIPAL ADVISOR: ASSOC. PROF. TANVAA TANSATIT, M.D., 66 pp.

Objective: To compare the efficiency of multiple electrodes radiofrequency ablation (RFA) combined with electrode replacements between switching multipolar and switching bipolar methods for creating an ablation area in ex vivo porcine livers.

Materials and Methods: We used a 330 kHz RF generator and three perfused needle electrodes to create 50 ablation zones by performing switching multipolar RFA ($n = 25$) or switching bipolar RFA ($n = 25$) in explanted porcine livers. In both methods, ablation areas were created by applying radiofrequency (RF) energy to the perfused needle electrodes in three sessions for 12, 10 and 8 minutes, respectively (total time = 30 minutes). The changes in the current, power output, voltage output and liver temperature during RFA, as well as the diameters, volume and shape of the thermal ablation zones, were compared between the two groups.

Results: In the switching multipolar and switching bipolar groups, the mean final-temperature values were $74.92 \pm 7.41^{\circ}$C and 70.92 ± 8.82 °C, respectively ($p = 0.089$). The switching multipolar mode created a larger volume of ablation than did the switching bipolar mode: 156.51 ± 26.81 cm^3 and 125.49 ± 29.72 cm^3, respectively ($p < 0.000$).

Conclusion: For the multiple electrodes RFA, the switching multipolar method was more efficient in generating larger areas of thermal ablation than the switching bipolar method.

Field of study Medical Science Student's signature Jutamart Pupud.
Academic year 2007 Principal Advisor's signature Tanvaa Tansatit

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LIST OF ABBREVIATIONS

A = Ampere

$^\circ$C = Celsius degree

cm = centimeter

cm^3 = centimeter cubic

Dmax = maximum diameter

Dmin = minimum diameter

Dv = vertical diameter

et al. = et alii

g = gram

IVC = Inferior Vena Cava

kHz = kilohertz

min = minute

ml = milliliter

mm = millimeter

NA = not applicable

NaCl = sodium chloride

RF = Radiofrequency

RFA = Radiofrequency Ablation

s = second

V = Volt, Voltage

W = Watt

¶ = Pie

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CHAPTER I

INTRODUCTION

1. Background and Rationale

Performing resection of malignant liver tumors has been used to treat patients suffering with liver cancer recently, but many of the patients' tumors are surgically unresectable either because of unfavorable anatomy or their poor hepatic functional reserve. Radiofrequency ablation (RFA) is a therapy option for the treatment of primary and secondary tumors. It has been used successfully in the treatment of the liver [1, 2], lung [3], bone [4], breast [5], and kidney [6]. This technique destroys tumors by heat with minimal invasive treatment because it used a small needle electrode with an insulated shaft inserted into the tumor percutaneously [7, 9], via laparoscopy [8, 9] or laparotomy [9].

In general, the percutaneous approach to RFA under ultrasound guidance was used for patients at high risk of complications with laparoscopic or open RFA. The laparoscopic or open RFA approach was used more frequently for potentially curative intent. Laparoscopic RFA was selected for patients with relatively smaller, superficially located, or easily accessible tumors that could not be treated under ultrasound guidance. Open surgical RFA was selected for patients with large tumors, a larger number of tumors, or deeply located tumors [9].

Monopolar RFA, which the current flows between an active electrode and a neural electrode through the body of the patient, is the most popular ablation technique, despite development of several devices for monopolar RFA, such as an internally cooled electrode (Radionics, Burlington, MA), a perfused electrode (Berchtold, Tuttlingen, Germany), and a multitined expandable electrode (LeVeen; Boston Scientific, Natick, MA). These devices induce coagulation necrosis in the range of 3-4 cm in diameter after only a single ablation and this technique has been shown to be highly effective in achieving coagulation in tumors smaller than 3 cm in diameter [10-15]. Adequate treatment of hepatic malignancies requires ablation of the entire tumor, including a sufficient safety margin of at least 1 cm to avoid local recurrence. However, monopolar RFA technique often results in failure to create a safety margin of tumor larger than 4 cm in diameter [16-18].

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In clinical procedure, multiple overlapping is a general method that used for larger liver tumors because of its comfortable process. The electrode was inserted anywhere into the locations of the tumors and then the generator delivered the current until the ablation spheres covered the entire tumors completely. Thereafter, some prior studies have performed a computer analysis of the size of the thermal area created by overlapping multiple ablation spheres; one ablation sphere was produced by a single placement of the RF electrodes, to describe protocol for treatment of larger liver tumors [42-43]. The results of the study showed the success rate of the treatment of 87.6% at the tumor size range of 3.6-7.0 cm [43]. However, to achieve the completed ablation spheres, this protocol has more number of electrode placements than other protocols.

Several methods by which lesion size have been investigated. These include saline-enhanced RFA [19], bipolar RFA [20-25], multipolar RFA [26-30], and switching monopolar RFA [1, 31-35]. Bipolar RFA, which both electrodes are located on one application instrument, has been developed to overcome the limitations of monopolar RFA and have already demonstrated their effectiveness and safety in experimental studies [20-23]. In bipolar mode, no grounding pad is required; this technique decreases the risk of possible skin burn at the grounding pad location due to high power densities in monopolar mode [36]. Several previous studies have demonstrated that bipolar RFA, compared to monopolar RFA, could create larger lesion because of a high and constant electric field gradient between the two electrodes [20-21, 23, 37-39]. Moreover, saline-enhanced RFA showed better performance in creating a large ablation zone than dry RFA owing to the high electrical conductivity of the saline [40-41]. However, prior studies have demonstrated that bipolar RFA has the limitation of creating non-spherical shaped ablation zones [21].

One way to overcome the limitation of bipolar RFA is the multipolar RFA approach, which uses three electrodes of internally cooled electrodes [26, 35] and multiple cooled cluster electrodes [32] are placed in triangular arrays with equidistant inter-electrode spacing. Previous studies used multipolar RFA technique in various modes such as sequential, simultaneous and switching monopolar modes, and they have demonstrated that switching mode, compared to sequential and simultaneous modes, could create larger and spherical shaped areas [26, 31-32, 34]. Moreover, switching monopolar method with a single application of multiple probes could decrease treatment time, procedure and anesthetic risks in many cases [33]. However, these studies, monopolar electric mode, required grounding pads to complete the circuit; it is possible that patients could be at greater risk for burns.

In the RFA with multiple electrodes, the current delivery could flow in several patterns. Previous study performed multiipolar RFA with three electrodes of internally cooled electrodes [26]. In that study, one electrode was used as an active electrode and it was connected to the generator RF output, and the others were used as dispersive electrodes, and they were connected to the generator “ground” output; therefore, all the current originating from one electrode entered the second and third electrodes and there was a high and constant electric field gradient between the active and dispersive electrodes. Moreover, the RFA with three electrodes could perform in bipolar electric mode. In this mode, one electrode was used as an active electrode and another one was used as a dispersive electrode; therefore, the current originating from one electrode entered the second electrode and there was a high electric field gradient between a pair of electrode. But, in some case, one electrode could not originate the current same as the other; so, the area of ablation was not spherical.

Therefore, this research focuses on methods of hepatic radiofrequency ablation combined with electrode replacements to create larger ablation zones. The purpose of this research is to compare the efficiency of hepatic radiofrequency ablation combined with electrode replacements in switching multipolar mode and switching bipolar mode for creating ablation zone in ex vivo porcine livers.

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2. Research Questions

2.1 Primary research question

How the diameters and volumes of ablation areas of the multiple electrodes RFA combined with electrode replacements in the switching multipolar mode and switching bipolar mode are?

2.2 Secondary research question

How the shape of ablation areas of the multiple electrodes RFA combined with electrode replacements in the switching multipolar mode and switching bipolar mode are?

3. Objectives

3.1 To compare the diameters and volumes of ablation areas of the multiple electrodes RFA combined with electrode replacements in the switching multipolar mode and switching bipolar mode in ex vivo porcine livers.

3.2 To examine the shape of ablation areas of the multiple electrodes RFA combined with electrode replacements in the switching multipolar mode and switching bipolar mode.

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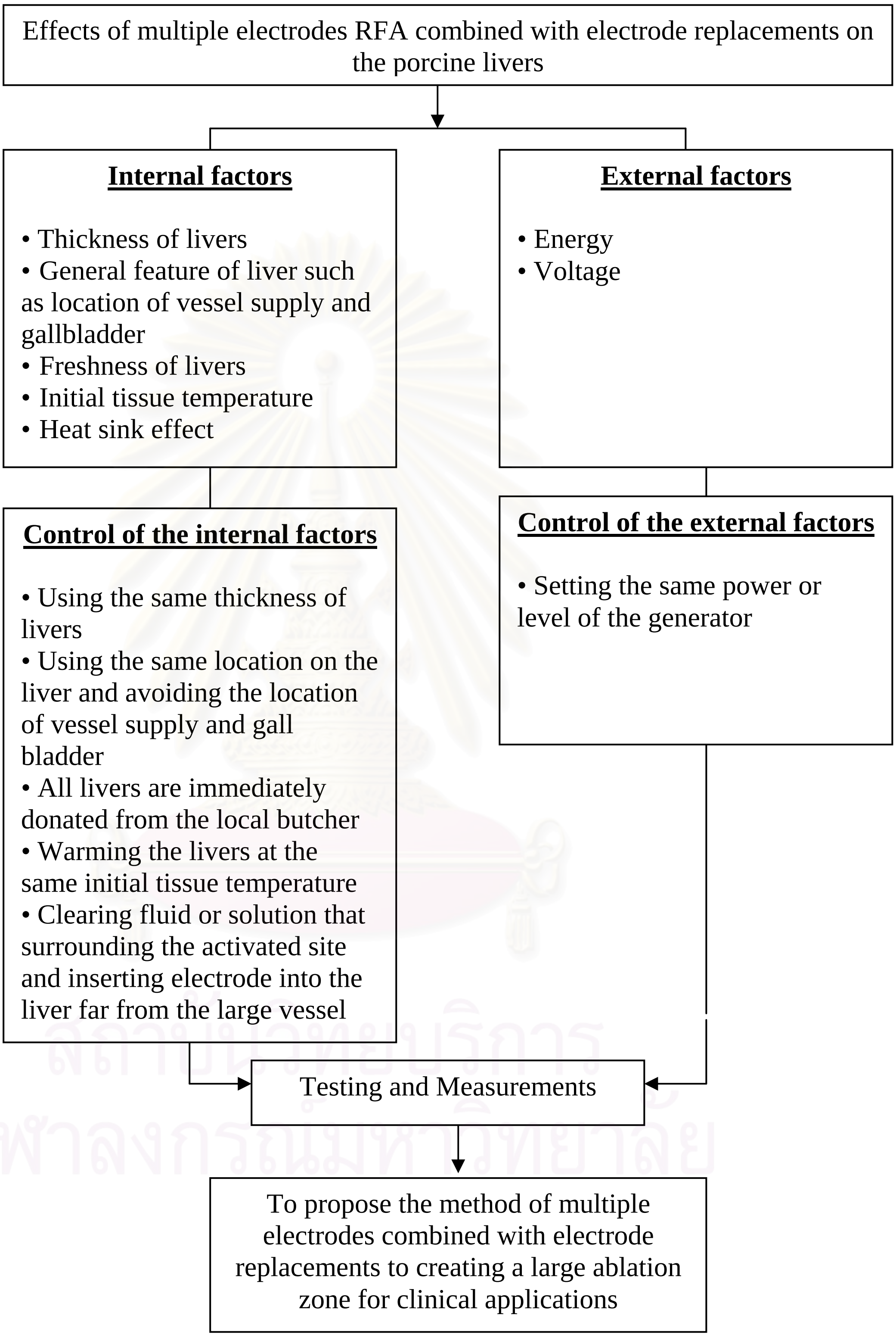
4. Conceptual Framework



Effects of multiple electrodes RFA combined with electrode replacements on the porcine livers

Internal factors

- Thickness of livers
- General feature of liver such as location of vessel supply and gallbladder
- Freshness of livers
- Initial tissue temperature
- Heat sink effect

External factors

- Energy
- Voltage

Control of the internal factors

- Using the same thickness of livers
- Using the same location on the liver and avoiding the location of vessel supply and gall bladder
- All livers are immediately donated from the local butcher
- Warming the livers at the same initial tissue temperature
- Clearing fluid or solution that surrounding the activated site and inserting electrode into the liver far from the large vessel

Control of the external factors

- Setting the same power or level of the generator

Testing and Measurements

To propose the method of multiple electrodes combined with electrode replacements to creating a large ablation zone for clinical applications

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5. Assumptions

1. The measurement has validity and reliability.

2. No impairments on the porcine livers.

6. Key Words

Radiofrequency ablation, switching multipolar mode, switching bipolar mode

7. Operational Definitions

1. Multiple electrodes RFA: The passage of high frequency alternating electric current through the patient’s body to create a desired surgical effect with use of more than one electrode.

2. Switching mode: The current flows to the electrode by using a switching box to switch the current between electrodes, from one electrode to the next electrode.

8. Obstacles

The research uses the porcine livers which purchased from the local butcher. The amount of the liver is about 2-3 livers for testing in a day so it can not test all ablation lesions in the same day, that can make the research delayed. Each lobe of the liver has not the same thickness so; the research will use many livers for choosing the appropriated lobe to test.

9. Expect Benefits and Applications

This research presents the efficiency of the multiple electrodes RFA combined with the electrode replacements in the switching multipolar and switching bipolar modes. The purposes of this research are that these methods can be applied to use in appropriated clinical procedures and create the better performance of the treatment for liver tumors. Moreover, these methods can not

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only decrease the treatment time but also increase the success rate of the treatments.

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CHAPTER II

REVIEW OF RELATED LITERATURES

1. General Features of Human and Porcine Livers

1.1 Human Liver

The human liver weight approximately 1500 g and accounts for approximately one-fortieth of adult body weight (Fig. 1). It lies in the right and left upper quadrants (mainly on the right side: right hypochondriac and epigastric regions of abdomen), inferior to the diaphragm which separates it from the pleura, lungs, pericardium, and heart. In addition to its many metabolic activities, the liver stores glycogen and secretes bile [51].

1.1.1 Surfaces of the liver

1.1.1.1 Diaphragmatic surface is smooth and dome-shaped where it is related to the concavity of the inferior surface of the diaphragm.

1.1.1.2Visceral surface is covered with peritoneum, except at the bed of the gallbladder and the porta hepatic, where vessels and ducts enter and leave the liver. It is related to

- Right side of the anterior aspect of the stomach- the gastric and pyloric areas
- Superior part of the duodenum- the duodenal area
- Lesser omentum
- Gallbladder
- Right colic flexure and right transverse colon- the colic area
- Right kidney and suprarenal gland- the renal and suprarenal areas

1.1.2 The hepatic lobes

1.1.2.1 Anatomical lobation: falciform ligament separated liver into two lobes;

- Left lobe: includes the caudate lobe and most of the quadrate lobe. The anatomical left lobe is separated from these lobes on the visceral surface by the fissure for the round ligament of the liver and the fissure for the

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ligamentum venosum, and on the diaphragmatic surface by the attachment of the falciform ligament.

- Right lobe: is demarcated from the left by gallbladder fossa inferiorly and the fossa for the inferior vena cava (IVC) superiorly.

1.1.2.2 Functional / Surgical lobation: Within each part the primary branchings of the portal vein and hepatic artery are consistent enough to form vascular segments (Fig. 2).

1.1.3 Vessels of the liver

The liver receives blood from two sources:

1.1.3.1 The portal vein (70%), a short, wide vein, is formed by the superior mesenteric and splenic veins posterior to the neck of the pancreas, ascends anterior to the IVC, and left branches that ramify within the liver.

1.1.3.2The hepatic artery (30%), a branch of the celiac trunk may be divided into the common hepatic artery and hepatic artery proper.

1.2 Porcine Liver

Liver is the largest organ in the body (Fig. 3). It is an extramural digestive gland of substantial importance in metabolism. Situated between the vessels draining the intestines and general circulation, the liver has many complex functions. The liver is in the abdominal cavity, abutting the diaphragm. The caudate process encloses the cranial pole of the right kidney in the right dorsal abdomen. Three distinct landmarks are used to orient the liver once it is removed from the body cavity [45]:

- *Caudal vena cava* runs through the dorsal portion of the liver.
- *Porta* the area where the vessels and nerves enter the organ on the visceral surface.
- *Renal impression* the indentation for the right kidney on the liver’s right side.

1.2.1 Lobes of the porcine liver

Deep fissures divide the liver into four basic lobes [50]:

- Right Lateral Lobe
- Left Lateral Lobe
- Right Median Lobe
- Left Median Lobe

1.2.2 Blood supply of the porcine liver

The liver has a dual blood supply:

1.2.2.1 Functional blood comes to the liver via the portal system, and brings nutrients freshly absorbed from the gut. It accounts for about ¾ of the blood flow to the liver.

1.2.2.2 Nutrient blood (oxygenated) comes from the hepatic artery to keep the hepatocyte alive.

Both types of blood empty into the liver sinusoids. Blood in the sinusoids empties into central vein, then into hepatic veins, that empty into the caudal vena cava.

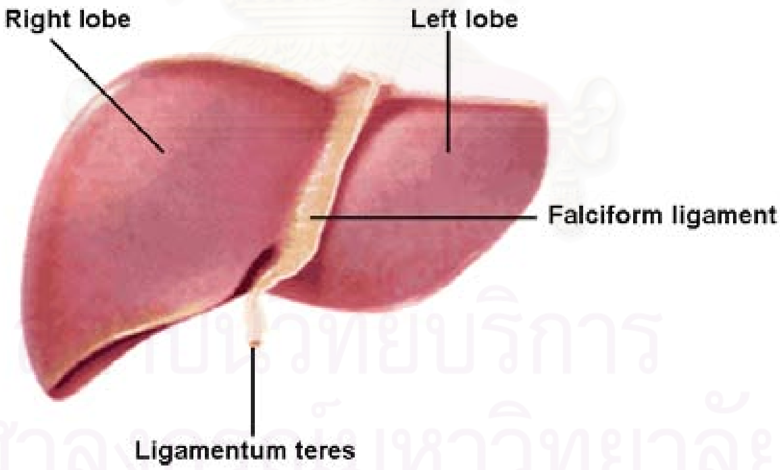

Figure 1. Surfaces of the human liver. Diaphragmatic surface is dome-shaped and conforms to the inferior surface of the diaphragm. Visceral surface with the impressions formed by the structures with which it is contact.

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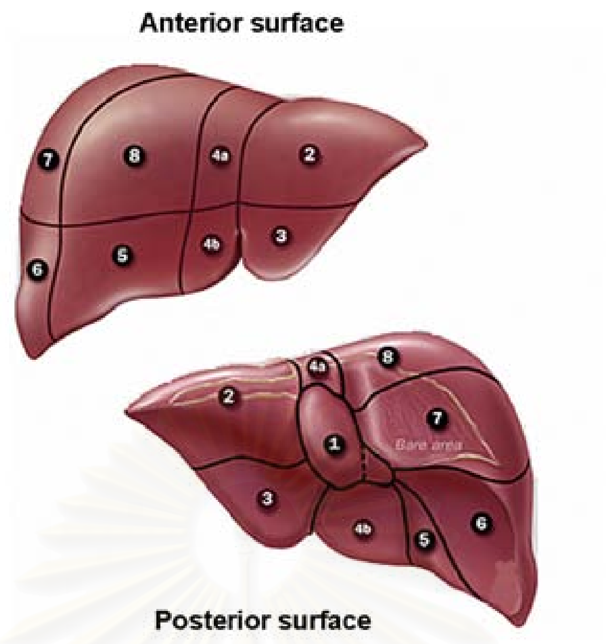

Figure 2. The segmentation of the human liver is based on the principal divisions of the hepatic artery and portal vein.

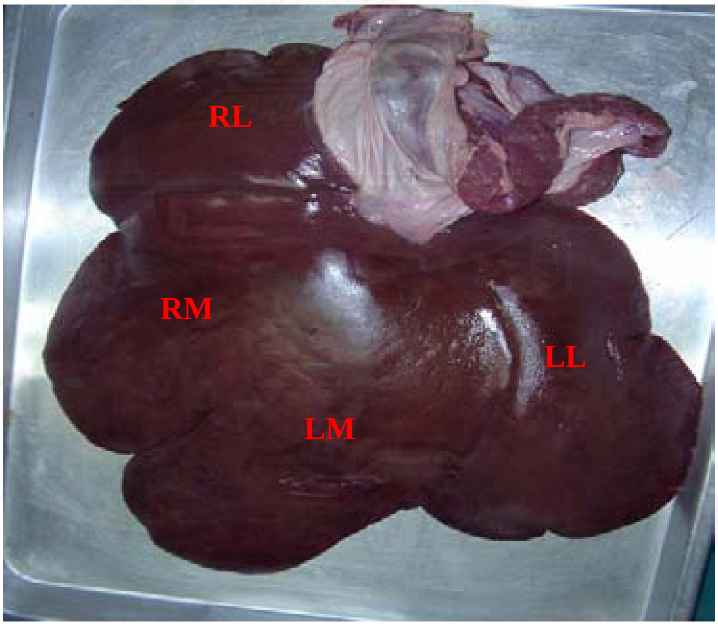

Figure 3. The porcine liver. Deep fissures divide the liver into four basic lobes; right lateral lobe (RL), left lateral lobe (LL), right median lobe (RM), and left median lobe (LM).

2. Hepatic Radiofrequency Ablation Using Multiple Electrodes System

2.1 Number and Types of Electrodes Used

An RFA system with multiple electrodes can consist of two (dual), three (triple), four (quadruple) or more electrodes [46]. Several previous studies have been used two electrodes to perform RFA system in bipolar and monopolar techniques [12, 14, 21-25, 33, 37-39]. Haemmerich et al. [14], in 2001, used two RITA 4-prong 15-gauge probes (model 30, RITA Medical Systems) for creating monopolar and bipolar lesions in domestic pigs for the in vivo experiments and examined the new bipolar RFA method. The result showed that bipolar RFA exhibited superior performance compared with monopolar RFA, creating lesions about three times as large. In 2003, Lee Jr et al. [33] described a prototype electrical switching circuit by using two RITA model-90 multiple prong probes which are extended to 3 cm. The RFA performed in an alternating monopolar method compare with conventional single probe to heat pig liver. The result from this study showed no differences between minimum diameter, maximum diameter and lesion volumes. All lesion shapes in this study were near spherical with some distortion from adjacent large blood vessels. Furthermore, in 2004, Lee et al. [22] performed the RFA systems with used two 15-gauge perfused-cooled electrodes to demonstrate the efficacy of the dual bipolar RF system for inducing coagulation necrosis in ex vivo bovine liver. The result showed coagulation necrosis in the large volume produced by the perfused-cooled electrode. In the next year, Lee et al. [24] have been investigated the efficacy of two RFA systems, the Berchtold RFA system which used two 16-gauge open-perfused electrodes with a tip exposure of 2 cm and the Radionics RFA system which used two 15-gauge cooled-wet electrodes with a tip exposure of 2 cm. They concluded that cooled-wet electrode induces a larger volume of tissue coagulation than open perfused electrode.

The prior studies have been reported the used of three electrodes in RFA systems. In 2005, Frericks et al. [27] used three internally cooled bipolar coagulation probes with an active tip length of 20, 30, or 40 mm and diameter of 1.8 mm to perform RFA system to treat 12 patients with liver tumors. In this case, when three bipolar probes were placed in a tumor, up to 15 possible combinations (pairs of electrodes) between the current may have passed. In 2006, Ritz et al. [28], Hacker et al. [29], and Clasen et al. [30] used three of the same bipolar probes in the study of Frericks et al. to perform the RFA with multiple electrodes for creating coagulation necrosis. Furthermore, Laeseke et al. [34] evaluated multiple-electrode RFA system by used three single electrodes, 17-gauge in diameter with 3-cm-long exposed tip, for creation of confluent areas of hepatic coagulation. Moreover, Haemmerich et al. [32] performed multiple cooled cluster electrodes in three clusters with using three single cool-tip electrodes (Cool-Tip; Radionics, Burlinton, Mass) for each cluster. Each cluster electrodes were inserted into the liver 4 cm apart in triangular configuration. However, in 2001, de Baere et al. [47] compared the RFA system between the cooled-needle radiofrequency system with a 17-gauge monopolar cooled triple-cluster needle electrode and the expandable needle radiofrequency system with a 15-gauge needle contains four hooks. They demonstrated that the cooled-tip needle induced significantly larger lesions than the expandable needle, but the lesions produced by the expandable needle are more reproducible, uniform, and spherical. From these systems, using three electrodes, the result showed the better efficiency to create the larger and more spherical shaped ablation area than the systems that used two electrodes.

From these several previous studies, the results showed that multiple-electrode RFA system could perform with various numbers and types of the electrodes. The best results were presented in the system which used more than two electrodes. Type of electrodes was varied for the appropriated procedure. Many clinical studies have been reported the used of multitined expandable electrode [48-49] because it could produce more oval lesion than the other electrodes. Nevertheless, this research uses three perfused needle electrodes for the multiple-electrode RFA system. Because of the conductivity of hypertonic saline, the RFA with perfused needle electrode can produce the larger ablation area than multitined expandable electrode.

2.2 Electric Mode

A multiple-electrode RFA system can be used in:

2.2.1 Monopolar mode: The electric current flows from all the electrodes that have the same polarity towards the grounding pad (Fig. 4).

2.2.2 Bipolar mode: The electric current flows between two parallel inserted electrodes or groups of electrodes (Fig. 5).

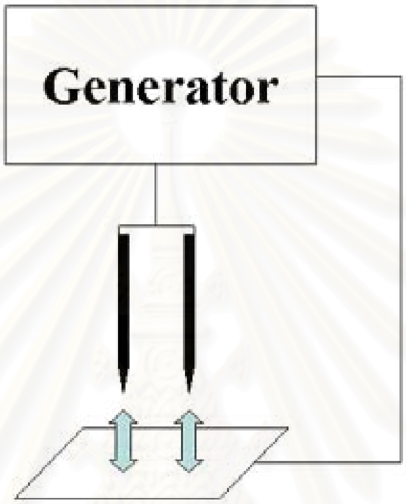

Figure 4. Monopolar System.

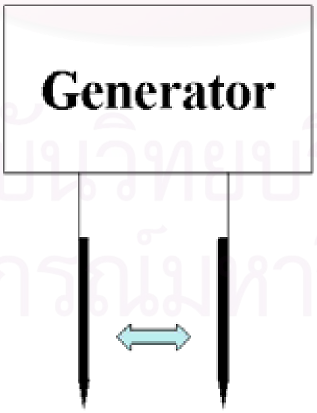

Figure 5. Bipolar system.

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Haemmerich et al. [14], in 2001, used two RITA 4-prong 15-gauge probes (model 30, RITA Medical Systems) for creating monopolar and bipolar lesions in domestic pigs for the in vivo experiments. This study reported that lesion volumes of monopolar ablation and bipolar ablation were 3.9 ± 1.8 cm^3 and 12.2 ± 3 cm^3, respectively. The finite element method of this study showed a mushroom shaped lesion in monopolar model while a cylinder shaped lesion in bipolar model.

Bipolar electric mode does not require a grounding pad; so, it has lower risk for burn than monopolar mode. However, many clinical procedures favored monopolar mode to created ablation zones because of comfortable technique of the treatment. But even so, this research determines the efficiency in the term of coagulation area induced from the switching multipolar and bipolar RFA system. The multipolar mode is similar to the bipolar mode because it does not require a grounding pad.

2.3 Activation Mode

A multiple-electrode RFA system can be activated in:

2.3.1 Consecutively or sequentially: The second electrode is activated after completion of the session of the first electrode (Fig. 6).

2.3.2 Simultaneously: The synchronous parallel electrical current flows to all electrodes (Fig. 7).

2.3.3 Switching or alternative: Using a switching box to switch the current between electrodes, from one electrode to the next electrode (Fig. 8).

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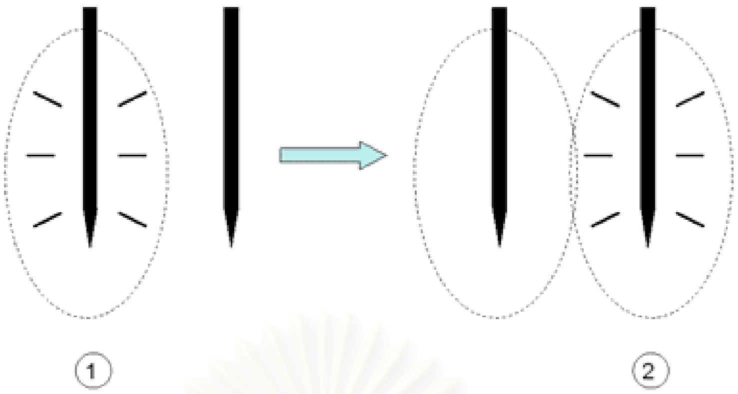

Figure 6. Consecutively or sequentially activation mode.

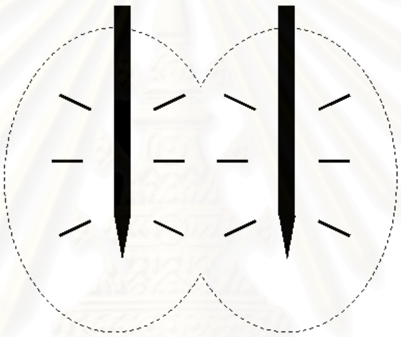

Figure 7. Simultaneously activation mode.

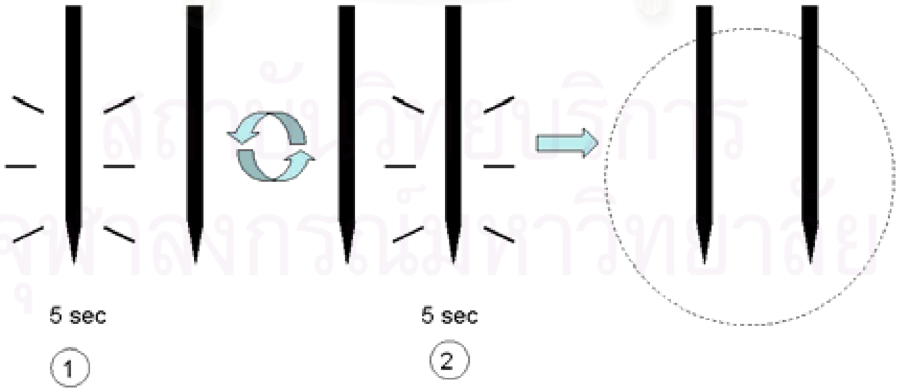

Figure 8. Switching or alternative activation mode.

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In 2004, Lee et al. [12] used two 17-gauge internally cooled electrodes with a 3-cm active tip (Radionics) for creating RF-induced coagulation lesions in multiple probe application and alternative RF application between the two electrodes by using a prototype switching adaptor. Their study applied RF energy to bovine livers in the sequential mode, the simultaneous mode, and the alternative mode. The results showed the alternative mode creates larger, more regular ablation zones than either the sequential or simultaneous mode.

Subsequently, in 2005 Haemmerich et al. [32] performed RFA system with cool-tip cluster electrodes in three clusters. The lesions were created with sequential method, simultaneous method, and rapid switching method. This study indicated that rapid switching created large round lesions and reduced treatment time. Moreover, the result represented small discontinuous lesions in simultaneous method.

Besides the above studies, in 2006 Lee et al. [26] compared the efficiency of multiple-electrode RFA in the consecutive mode, the simultaneous mode, and the multipolar mode. They concluded that the multipolar RFA was more efficient in generating larger areas of thermal ablation than either the consecutive or simultaneous modes. Their study results suggested that when treating large tumors, they proposed multipolar RFA using triple probes destroy tumors with a single application and with a reduced treatment time.

From the results of the previous studies, this research will use switching mode in the multiple-electrode RFA system to create the coagulation areas.

2.4 Inter-electrode Distance

In 1998, Goldberg et al. [35] performed ex vivo liver experiments in four distinct phases. In phase 1, they determined the optimal RF electrode spacing at which an array of three equidistance electrodes could produce a uniform circular cross-sectional area of coagulation necrosis. They inserted internally cooled electrodes with 2-cm-long tip exposure into the liver 0.5, 1.0, 1.5, 2.0, 2.5, or 3.0 cm apart and applied RF energy for 10 minutes. Showing the result of 3 cm spacing of the array, three individual lesions with a mean diameter of 2.5 ± 0.1 cm were seen. The volume of coagulation necrosis did not become spherical until 0.5 or 1.0 cm spacing was used and these spacing produced 4.1 ± 0.2 cm in diameter.

In 2001, Haemmerich et al. [14] performed preliminary in vivo experiment with bipolar configuration of mutiprong electrodes at probe distances of 3.5, 3, and 2.5 cm. They reported that when the distance was 3.5 and 3 cm, in some cases they found a gap of viable tissue between two lesions. So, they used 2.5 cm probe distance in their main experiment.

In 2005, Haemmerich et al. [32] compared three methods of creating large thermal lesions by using three cool-tip cluster electrodes with an exposed length of 2.5 cm inserted into the liver 4 cm apart in triangular configuration. The thermal lesions resulting from this experiment showed the rapid switching method created one large and uniform lesion with a mean maximum diameter of 6.8 ± 0.9 cm, whereas the simultaneous method results in three small and discontinuous thermal lesions; so, it could not measure a maximum diameter. In the sequential method produced trilobed, clover leaf-shaped lesions with a mean maximum diameter of 7.3 ± 0.7 cm.

In addition, in 2006, Clasen et al. [30] evaluated the size and geometry of thermal lesion by using three bipolar applicators in an equidistant array at 2, 3, 4, or 5 cm and various power output (75, 100, 125, 175, or 225 W). Induced coagulations were confluent for inter-applicator distances of 2, 3 cm (75-225 W), 4 cm (75-125 W), and 5 cm (75-100 W). Confluent zones were well defined and had regular shapes.

Furthermore, Lee et al. [26] compared the efficiency of multipolar RFA by using three perfused-cooled electrodes with multiple overlapping and simultaneous monopolar techniques. Their preliminary experiments were performed to find the ideal inter-electrode distance for creating a spherical-shaped ablation zone. Thermal ablation zones were created at 3, 4, and 5 cm inter-electrode distances. The results showed that the largest volume of coagulation necrosis was achieved at 4 cm spacing (75.9 ± 9.7 cm^3): 42.4 ± 7 cm^3 at 3 cm spacing and 47.6 ± 14 cm^3 at 5 cm spacing. In the pilot study, we used three perfused needle electrodes in an initial equidistant array at 3, 4, or 5 cm to create ablation areas. The results showed that the more spherical shape of ablation area was achieved at 4 cm inter-electrode distance.

From the previous studies and the pilot study, this research chooses 4-cm initial inter-electrode distance because of its efficiency to create more spherical shape of coagulation necrosis.

2.5 Switching Interval Time

In 2003, Lee Jr et al. [33] tested a new prototype multiple probe generator with a built-in switching mechanism to determine if multiple lesions can be produced in the same time that a single conventional ablation can be performed. They used two RITA model-90 multiple prong probes extended to 3.0 cm in this experiment. The probe output from the RF generator was routed to an electromechanical switch capable of switching between probes approximately every 0.5 second. No differences could be detected between minimum diameter of the RF lesion (1.63 ± 0.56 cm single versus 1.61 ± 0.53 cm dual; $p = .94$), maximum diameter (3.3 ± 0.84 cm single versus 3.4 ± 0.55 cm dual; $p = .79$) or lesion volumes (13.6 ± 9.3 cm^3 single versus 13.7 ± 7.0 cm^3 dual; $p = .97$).

Furthermore, in 2004, Lee et al. [12] explored the impact of the alternative mode on the area of induced coagulation necrosis compared with the sequential or simultaneous mode for the application of multiple probes RFA. In this study, the alternative mode applied the energy alternately to electrode by changing the current flow at a two-second interval. They concluded that alternative mode exhibited superior performance compared with other modes, and created larger lesion.

Subsequently, in 2005, Haemmerich et al. [32] compared three methods of creating large thermal lesions by using three cool-tip cluster electrodes. RF energy was switched between three cluster electrodes which the first cluster electrode was energized for 1 second, then the second cluster electrode was energized for 1 second, and so on. The results reported that the average lesion volume for the rapid switching method was 116.4 cm^3, which was more than five times larger than that for the simultaneous method. The rapid switching method created thermal lesions that were 15% smaller in volume (116.4 ± 15.2 cm^3) than were those for the sequential method (137.5 ± 22.2 cm^3, $p = .047$).

Moreover, in 2006, Laeseke et al. [34] prospectively evaluated an impedance-based multiple electrode RFA system for creation of confluent areas of hepatic coagulation by used three cool-tip electrodes placed 2 cm apart in an equilateral triangular configuration. Power was switched from one electrode to the next when the impedance spiked- that is, reached 30 ohm above the baseline level or reached a maximum time interval (baseline determined at 10 seconds). From this study, the mean minimum diameter, maximum diameter, and volume of the coagulation zones created with multiple-electrode ablation were significantly larger than those created with other methods at 16 minutes. Finally, they concluded that switching electrodes at fixed time interval is less efficient than using an impedance-controlled algorithm.

In 2007, Lee et al. [31] determined the optimal switching time to create a large coagulation zone in the liver by switching monopolar RFA technique with a different switching time at 5, 15, 30, and 60 seconds, respectively and three internally cooled electrodes were placed 3 cm apart in triangular array. This study showed the results of switching RFA volumes for 30 seconds and 60 seconds created larger ablation volumes than with 5 seconds and 15 seconds. However, as the RF application time increased, there was a tendency for the switching time to become less than 30 seconds due to the change of tissue impedance.

In the pilot study of this research, multiple-electrode RFA by using three perfused needle electrodes placed in triangular array with 4 cm initial inter-electrode spacing, at 5 or 10 seconds switching interval time showed that 10 seconds switching time caused the current dropout from the initial value more rapid than 5 seconds switching time. From this result, could assume that 10 seconds switching time is too long to use in the experiment because it induced rising of impedance of the tissue around the electrodes or tissue charring. So, the switching time at 5 seconds is appropriate than 10 seconds for using in this study.

2.6 Concentration and Rate of Saline Infusion

In 2005, Lee et al. [20] determined the appropriate concentration and volumes of perfused NaCl solution for the bipolar RFA. To find the ideal concentration, they performed bipolar RFA with instillation of 0.9%, 6%, 12%, 24%, and 36% NaCl solutions. To find the ideal instillation rates of hypertonic saline (a solution of 6% NaCl), they performed bipolar RFA with various instillation rates of hypertonic saline, i.e., 0.5 ml/min, 1.0 ml/min, and 2.0 ml/min. The results from this study showed that bipolar RFA created larger short-axis diameters of coagulation necrosis with 6% NaCl instillation (35.8 ± 15 mm) than with isotonic (0.9%) saline solution (17 ± 9.7 mm) ($p < 0.05$). However, they demonstrated that, higher concentrations of NaCl solution (above 6%) did not further increase the dimension of coagulation necrosis: 30.6 ± 16 mm (12%), 29.2 ± 11.4 mm (24%), and 36.2 ± 6 mm (36%) ($p > 0.05$). Regarding the ideal instillation rate of NaCl solution, bipolar RFA with 6% hypertonic saline at a rate of 1.0 ml/min (37.9 ± 5.4 mm) or 2.0 ml/min (35.6 ± 9.3 mm) produced a larger diameter between the electrodes in ablation area than did 0.5 ml/min (25.8 ± 9.3 mm) ($p < 0.05$).

From the previous study, 6% hypertonic saline solution instillation at a rate of 1.0 or 2.0 ml/min was showed the better performance to create a large ablation area. In the pilot study, we used normal saline and 3% hypertonic saline to create an ablation area. The result showed that 3% hypertonic saline could create a larger ablation area than normal saline. In this research uses 3% hypertonic saline solution because it is more available than 6% hypertonic saline solution in the hospital. The instillation rate at 6.0 ml/min is used in this study because of the availability of the syringe that used in syringe pump.

3. The Replacement of Electrodes

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In 2001, Dodd et al. [42] performed a computer analysis of the size of the thermal injury created by overlapping multiple thermal ablation spheres with the electrode reposition. They used a computer-assisted design system to create three-dimensional models of spherical tumor and then analyzed the effect of size and geometric configuration of the ablation spheres. The results showed the single-ablation model, six-ablation model, 14-ablation model, and cylindrical ablation model (27 spheres). They demonstrated that, these model could be used to treat larger tumors because they could be covered the larger tumors with a tumor-free margin. So, they can decrease the risk of recurrent rate of the tumors.

In addition, Chen et al. [43], in 2004, established a preoperative protocol for ultrasonographically guided percutaneous RFA of large liver tumors that is based on mathematic models. Then, they performed the clinical application in 110 patients with hepatic tumors to evaluate the role of this protocol in RFA. In this protocol, one ablation sphere was produced by a single placement of the RF electrode. The RF device (Model 1500; RITA Medical Systems, Mountain View, Calif) that they used could produce 5-cm ablation spheres. Replacement of the electrodes was required when tissue was insufficiently ablated. From this study, the result presented a success rate of treatment for large tumors at 87.6%. Although this study had a higher success rate and could create a larger ablation area, it has been taken a longer treatment time than the other previous studies.

From the prior studies, this research will perform multiple-electrode RFA combined with electrode replacements to create a larger ablation zone and to decrease treatment time of the multiple overlapping ablation technique from the previous results.

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CHAPTER III

RESEARCH METHODOLOGY

1. Target Population and Sample Population

Livers of porcine models are purchased from a local butcher.

2. Inclusion Criteria

- Fresh porcine livers.
- No restriction on sexes and ages of porcine models.

3. Exclusion Criteria

- The decomposed porcine livers.

4. Sample Size Determination

In previous study of Haemmerich et al. [32], sixteen ablation zones were ablated with 2 multipolar RFA modes. The mean volume of the sequential mode was 137.5 ± 22.2 cm^3 and the switching mode was 116.4 ± 15.2 cm^3.

Continuous variables of two independent groups

$$n/\text{group} = 2(Z_{\alpha/2} + Z_{\beta})^2\sigma^2/(x_1 - x_2)^2$$

where; $Z_{\alpha/2} = Z_{0.05/2} = 1.96$ (two tail)

$Z_{\beta} = Z_{0.10} = 1.28$

σ^2 = Pooled variance

$= (n_1 - 1)\, S_1^2 + (n_2 - 1)\, S_2^2/\, (n_1 + n_2 - 2)$

$= 361.94$

so; $n/\text{group} = 2(Z_{\alpha/2} + Z_{\beta})^2\sigma^2/(x_1 - x_2)^2$

$= 2\, (1.96 + 1.28)^2\, (361.94)/\, (137.5 - 116.4)^2$

$= 17.068$

$\therefore$ The sample size was at least 18 ablation zones for each group.

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5. Materials

Radiofrequency ablation testing

- 330 kHz RF generator
- Switching box
- Spinal needle x 3
- Extension tube x 3
- Syringe 20 cc x 3
- Motor adaptor
- Thermocouple
- Acrylic plate with multiple holes at 5-mm intervals
- Calipers
- Stopwatch
- Hemostatic clamps x 2
- Operative scissors
- Operative knife
- Forceps x 2
- 3 % normal saline 500 ml x 24
- Latex examination gloves

Histological technique

- Tissue processing apparatus
- Hematoxylin-eosin stain
- Light microscope

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6. Methods

6.1 RFA Setting

Fresh porcine livers were immediately acquired from a local butcher. These livers were allowed to warm to room temperature (approximately 25^{o}C) before the experiment were conducted. For each experiment, one liver was used for 3 ablation lesions. A generator (330 kHz, Heat Intertrade Company Limited, Bangkok, Thailand) (Fig. 9A) was used at maximum wattage. The RFA was performed in three sessions for an ablation lesion. Three perfused needle electrodes in the diameter of 1.2 mm and the tip exposure of 2 cm (Fig. 10) were inserted into the liver in triangular arrays start with equidistant inter-electrode spacing at 4 cm and then changed to 5.5 cm in 60 degree rotary direction after the first session was completed. After that, the inter-electrode spacing changed to 7 cm in the next 60 degree rotary direction for the last session. The electrodes themselves were placed through an acrylic plate that contained. The tips of the electrodes were advanced at least 3 cm. into the target liver. One electrode was used as an active electrode and the others were used as dispersive electrodes in the switching multipolar group. In the switching bipolar group, one electrode was used as an active electrode and another one was used as a dispersive electrode. The delivery of the RF energy was performed by the switching box (Heat Intertrade Company Limited, Bangkok, Thailand) (Fig. 9B) in the switching multipolar group. Based on the pilot study, 3% NaCl was used as the perfusion solution with a flow rate of 6 ml/min by using the three syringe pumps. To continuously measure the local tissue temperature during the procedure, a thermocouple was inserted into the liver at the center of the triangle that connected each electrode. A total of 50 lesions were created by using switching multipolar group (n = 25) and switching bipolar group (n = 25). The two groups were activated in switching mode at the active phase of 5 seconds and the pause phase of 1 second. The first active electrode was energized for 5 seconds and pause 1 second, and then the second active electrode was energized for 5 seconds and pause 1 second, and so on in the third active electrode until ablation area was completed.

The applied current, voltage output, power output, local tissue temperature were recorded manually at the 1 minute interval during the RFA. The dimensions, volume and shape of the ablation area were compared for each group.

Figure 9. 330 kHz - RF generator (A) and switching box (B).

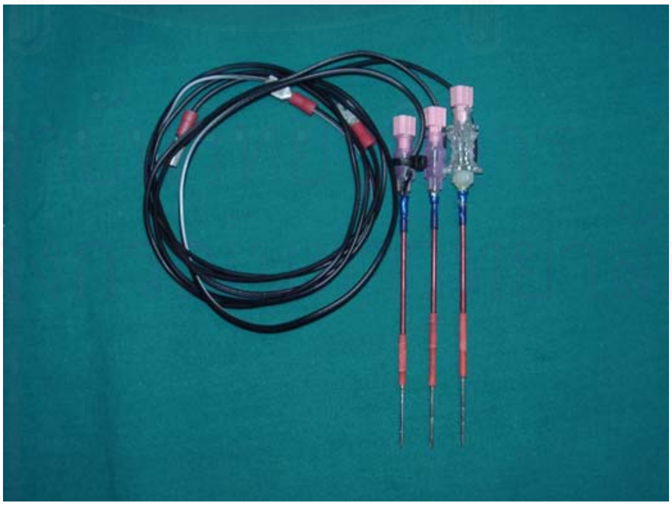

Figure 10. The perfused needle electrodes in the diameter of 1.2 mm and the tip exposure of 2 cm.

6.2 Ablation Protocol

6.2.1 Switching Multipolar Group

The system consisted of three perfused needle electrodes with a tip exposure of 2 cm and the 330 kHz generator (Heat Intertrade Company Limited, Bangkok, Thailand). Based on the pilot study of the optimal time in each session, the time in the first session was longer than the other sessions. The second and third sessions used decreasing time from the first session. So, three electrodes were inserted into the liver in triangular arrays with initial inter-electrode spacing at 4 cm and the RF energy was applied for 12 minutes in the first session. When the first session was complete, the second session would start with replace electrodes at 5.5 cm inter-electrode spacing and applied energy for 10 minutes. In the last session, the inter-electrode spacing was changed to 7 cm and applied energy for 8 minutes; thus, the total time required to create each lesion was 30 minutes. In this group, one electrode was used as an active electrode and the others were used as dispersive electrodes (1 active electrode and 2 dispersive electrodes; Fig. 11A).

6.2.2 Switching Bipolar Group

For this group, the experimental protocol was the same as the switching multipolar group. The difference between the two groups was the function of three electrodes. In the switching bipolar group, one electrode was used as an active electrode and another one was used as a dispersive electrode (1 active electrode and 1 dispersive electrode; Fig. 11B). So, the applied current flows between two electrodes for the activation. But, in the switching multipolar group, the applied current flowed from an active electrode to two dispersive electrodes for the activation.

6.3 Assessment of the Ablation Area

The livers were dissected along the plane perpendicular to the axis of the electrode insertion because the white central area of the RF ablation zone had been shown to correspond to the zone of coagulation necrosis [44]; so, the observer measured with calipers the maximum diameter (Dmax) and the minimum diameter (Dmin) of the central (Fig. 12A). The vertical diameter (Dv) was measured in an additional plane along the electrode tracks (Fig. 12B). The volume was calculated by using the formula: ¶ (Dv*Dmax*Dmin)/6. The shape of the ablation zone was characterized by the ratio between the maximum diameter and the minimum diameter (Dmax/Dmin) [31].

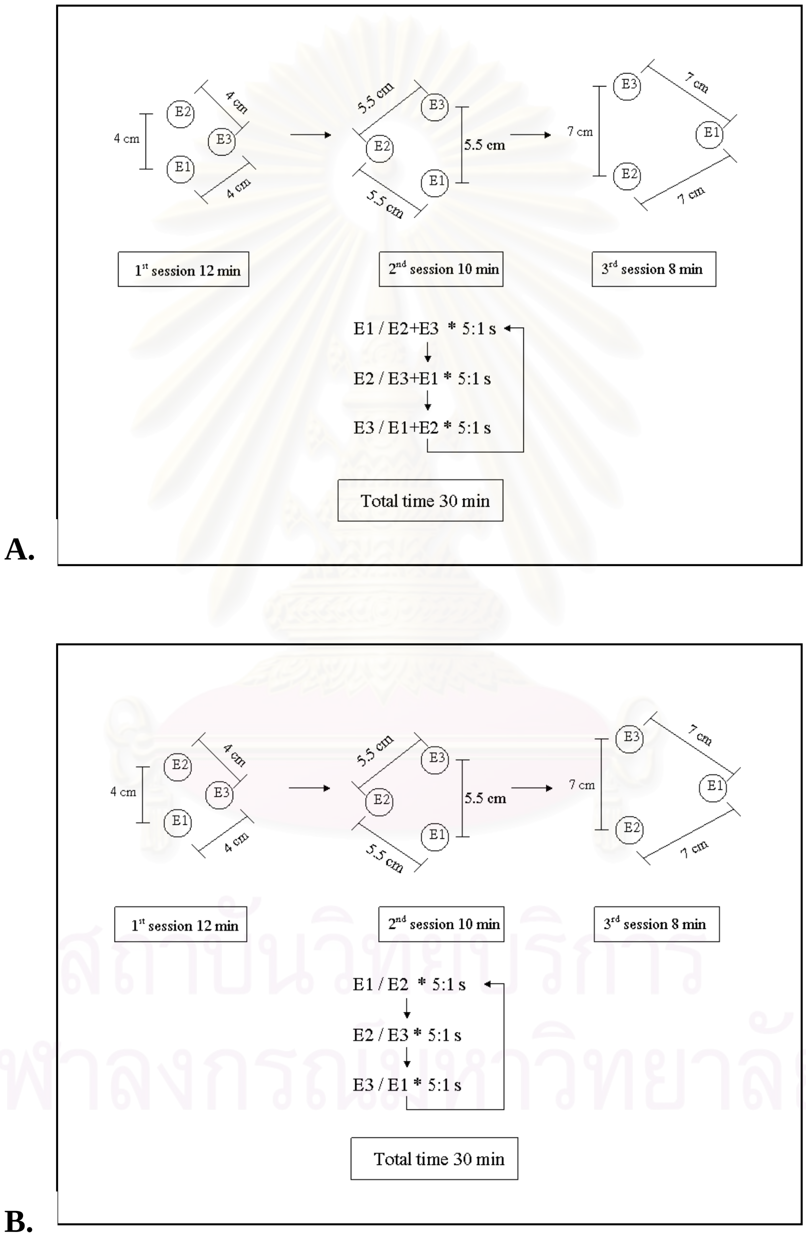

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Figure 11. Diagram of ablation protocol of switching multipolar group (A) and switching bipolar group (B). E = electrode, 5:1 s = active phase of 5 seconds and the pause phase of 1 second.

6.4 Histological Analysis

To confirm histologic findings of the ablated region, the RF-induced ablated regions in all cases were fixed in 10% formalin for routine histologic processing and were finally processed by paraffin sectioning and hematoxylin-eosin staning for light microscope study [44].

7. Data Analysis

The dimensions of the ablation areas and the technical parameters of the two groups were compared using the Student *t* test. For all the statistical analyses, a p value less than 0.05 was considered statistically significant. The statistics were performed using SPSS 11.0 computer software.

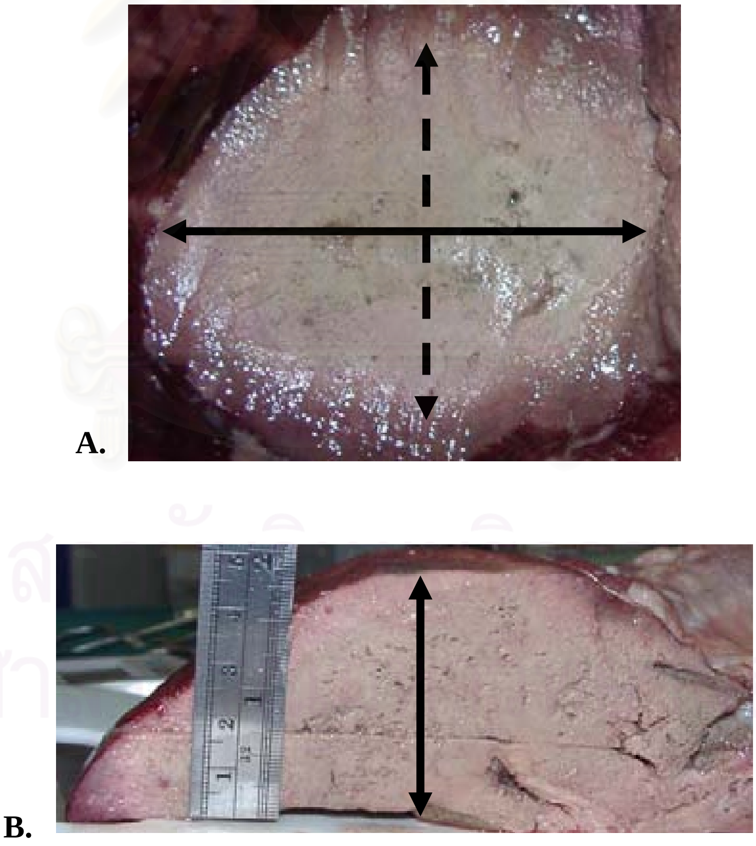

Figure 12. Assessment of the ablation area; (A) the maximum diameter (Dmax; dull line), the minimum diameter (Dmin; dot line) and (B) the vertical diameter (Dv).

CHAPTER IV

RESULTS

A total 50 lobes of porcine livers were studied for the diameters, volume and shape of the ablation lesions. Not only that, this research studied the other parameters such as the applied current, voltage output, power output, and local tissue temperature during the RFA that influenced the ablation lesion. Twenty five lesions were created by using switching multipolar group and the other 25 lesions were created by using switching bipolar group.

1. The Diameters of Ablation Lesion

Fifty lobes of porcine livers were ablated to evaluate the diameters of ablation lesion. The livers were dissected along the plane perpendicular to the axis of the electrode insertion and then measured with calipers the maximum diameter (Dmax) and the minimum diameter (Dmin) of the central (Fig. 13). The vertical diameter (Dv) was measured in an additional plane along the electrode tracks (Fig. 14).

After RFA, switching multipolar and bipolar methods created well-defined ablation lesions. All diameters of the ablation lesions in switching multipolar group were larger than switching bipolar group (Table 1). The mean maximum diameters (Dmax) of the lesions in switching multipolar and switching bipolar groups were 8.54 ± 0.44 cm and 8.12 ± 0.58 cm, respectively ($p = 0.006$). The mean minimum diameters (Dmin) of the two groups were as follows: 7.24 ± 0.48 cm in switching multipolar group and 6.93 ± 0.63 cm in switching bipolar group ($p = 0.057$). In addition, the mean vertical diameters (Dv) along the axis of the electrodes were 4.81 ± 0.59 cm in switching multipolar group and 4.22 ± 0.64 cm in switching bipolar group ($p = 0.001$). The difference in mean value of maximum diameter and vertical diameter of the coagulation between switching multipolar and switching bipolar groups were statistically significant.

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Table 1. The mean diameters of the ablation lesions created with switching multipolar and switching bipolar methods

Group	**Number of lesions**	**Mean maximum diameter(Dmax) (cm)**	**Mean minimum diameter(Dmin) (cm)**	**Mean vertical diameter(Dv) (cm)**
Switching multipolar	25	8.54 ± 0.44* (7.53-9.13)	7.24 ± 0.48** (6.23-8.33)	4.81 ± 0.59*** (3.73-5.77)
Switching bipolar	25	8.12 ± 0.58* (7.27-9.60)	6.93 ± 0.63** (5.40-7.93)	4.22 ± 0.64*** (3.07-5.17)

*p = 0.006, **p = 0.057, ***p = 0.001

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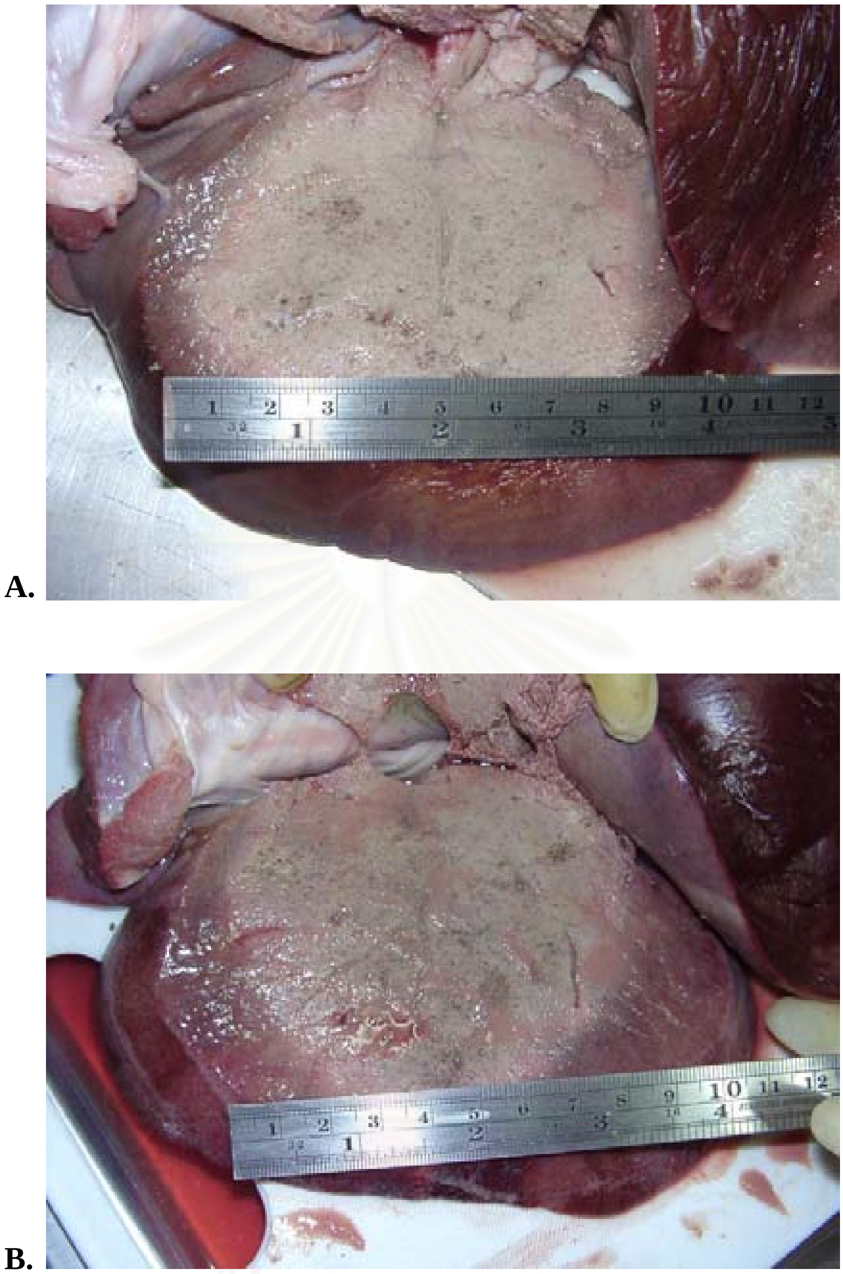

Figure 13. Cross sections of the ablation lesions creating with switching multipolar (A) and switching bipolar methods (B). The two methods created large round lesions.

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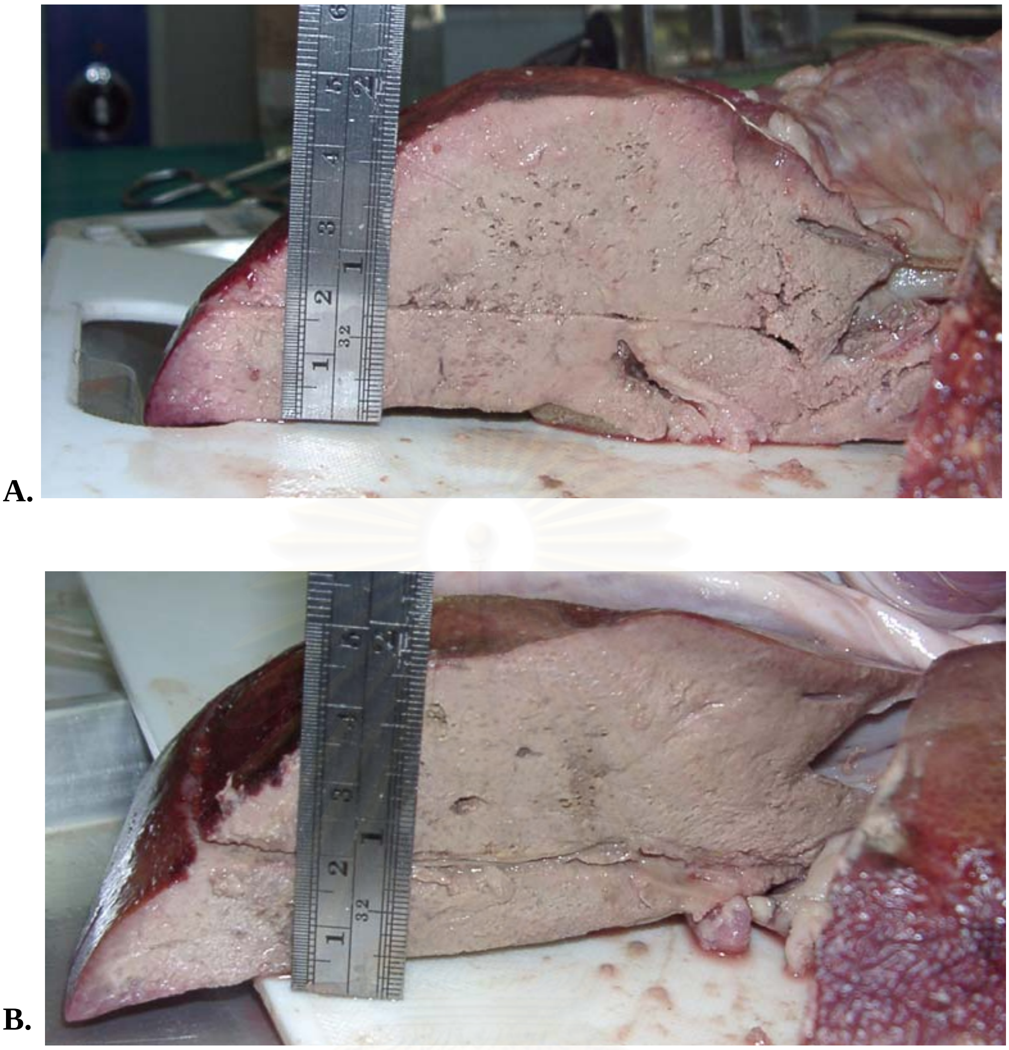

Figure 14. The vertical diameter of the ablation lesions created with switching multipolar (A) and switching bipolar methods (B).

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2. The Isometric Ratio and Volume of Ablation Lesions

The shape of each ablation lesion was evaluated using a rough estimate of lesion “roundness” in 2 dimensions by computing the isometric ratio for the transverse slice of each thermal coagulation zone. The switching multipolar and switching bipolar methods tended to produce round-shaped coagulation with a less prominent “waist” formation between the electrodes. The ratio that nearly 1 indicated the round shaped of ablation lesion. The mean ratio between the maximum and minimum diameter was 1.18 ± 0.09 in switching multipolar group and it was 1.18 ± 0.15 in switching bipolar group. The difference in mean value of the isometric ratio in both groups did not differ significantly (Table 2; p = 0.963).

Furthermore, the volumes of the ablation zones obtained with the switching multipolar and switching bipolar methods were 156.51 ± 26.81 cm^3 and 125.49 ± 29.72 cm^3, respectively, and the difference in the volume of the ablation lesions between the switching multipolar and switching bipolar groups was statistically significant (Table 2; p < 0.001).

Table 2. The isometric ratio and volume of ablation lesions

Group	**Isometric ratio**	**Volume (cm^3)**
Switching multipolar	1.18 ± 0.09* (1.02-1.32)	156.51 ± 26.81** (122.11-207.01)
Switching bipolar	1.18 ± 0.15* (1.04-1.78)	125.49 ± 29.72** (83.07-181.46)

*p = 0.963, **p < 0.001

3. Histological Findings

Histologically, the ablated regions in representative cases demonstrated the different appearance in three zones, a central necrotic zone, a marginal zone, and an untreated zone. A central necrotic zone surrounded by a marginal zone. There was a sharp demarcation between coagulated and untreated tissue. Within the central necrotic zone, densely hepatic cords were found and blood vessels shrank. Within the marginal zone, area of sinusoidal congestion was accompanied by advanced necrotic changes and patches of normal cells. However, the untreated zone contained normal hepatocytes (Fig. 15, 17). In addition, there were some

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cases of ablation areas that could not demonstrated in separated three zones. They appeared two different zones, central necrotic and untreated zones (Fig. 16).

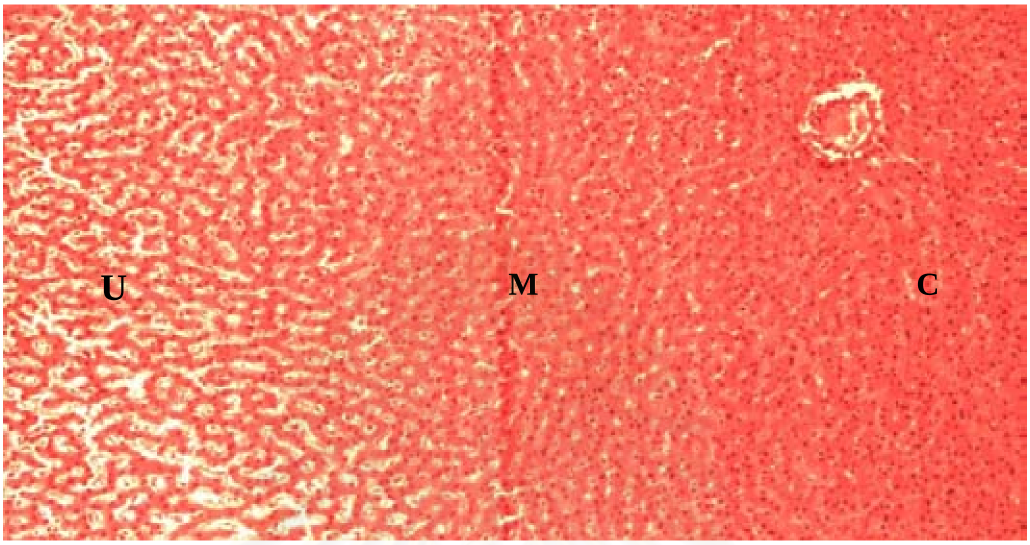

Figure 15. The hematoxylin and eosin stain of the liver revealed three zone lesions Zone C (central necrotic) consisted of necrotic tissue with densely architecture; zone M (marginal) was characterized by digesting necrotic tissue and patches of normal cells; and zone U (untreated) consisted of normal hepatocytes. Magnification: x 50.

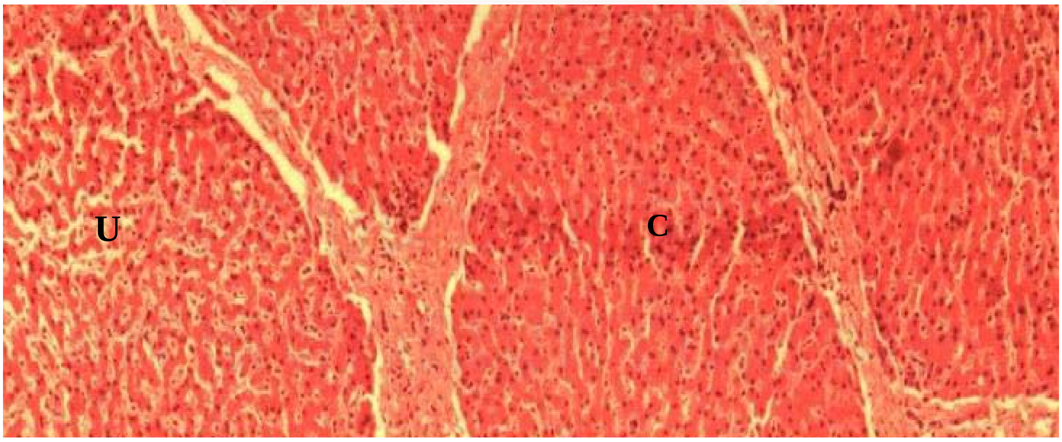

Figure 16. The hematoxylin and eosin stain of the liver appeared two different zones, central necrotic (C) and untreated (U) zones. Magnification: x 50.

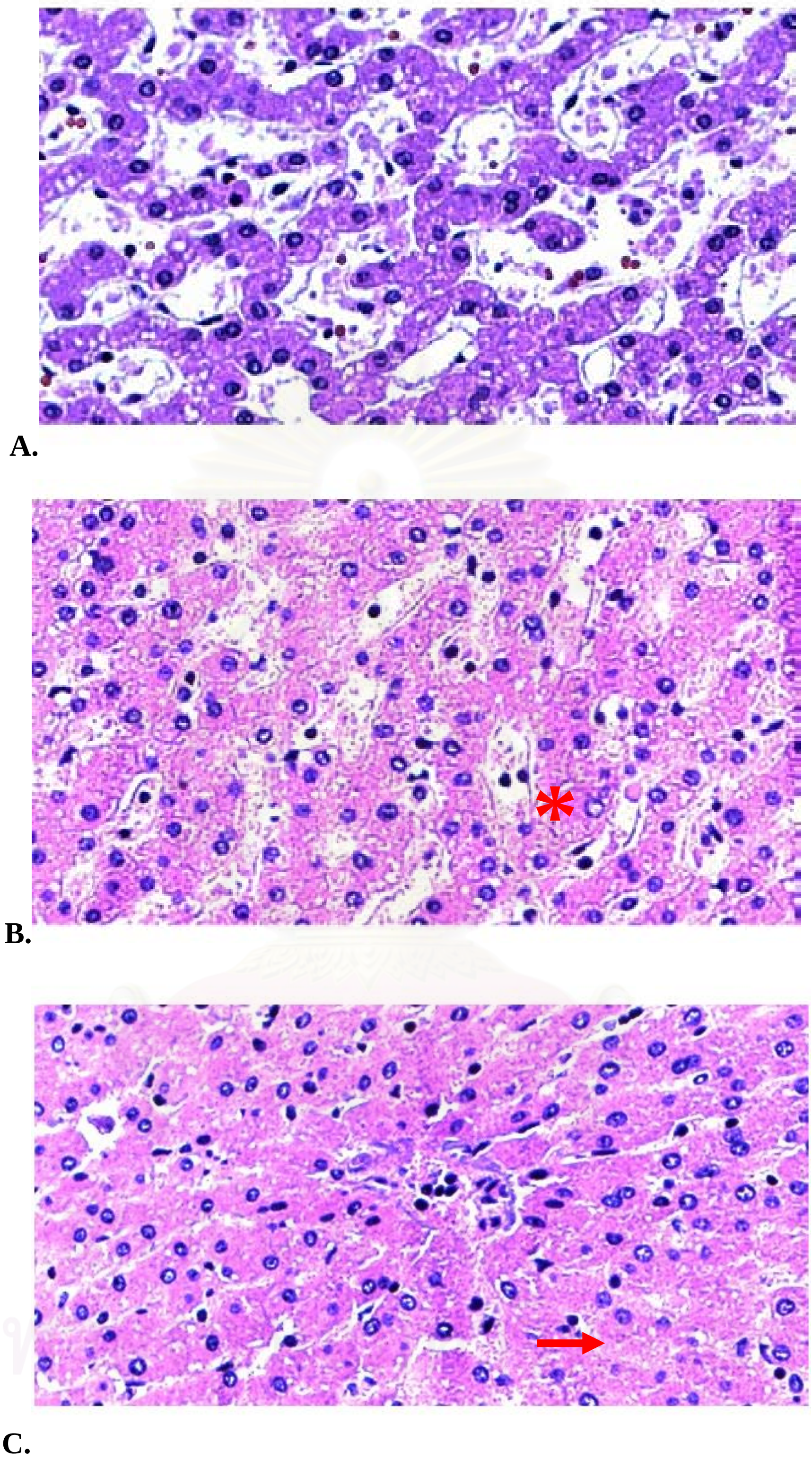

Figure 17. The hematoxylin and eosin stain of the three zone lesions; untreated zone (A), marginal zone (B) with some microvascular cell swelling (*), and central necrotic zone (C) with cells or tissue were converted into a dry, dull, fairly homogeneous eosinophilic mass and cell membrane disruption (arrow). Magnification: x 200.

4. Technical Parameters

The local tissue temperature before RFA was allowed approximately to the room temperature. Mean local tissue temperatures in switching multipolar and switching bipolar groups were 22.04 ± 1.86 °C and 20.88 ± 2.11 °C, respectively. The graphs in figure 18 show the mean temperature at the center portion of the inserted electrodes in all three sessions. In switching multipolar and switching bipolar groups, the mean final temperature values were 74.92 ± 7.41°C and 70.92 ± 8.82 °C, respectively (*p* = 0.089). The initial and final temperatures in each session were shown in table 3.

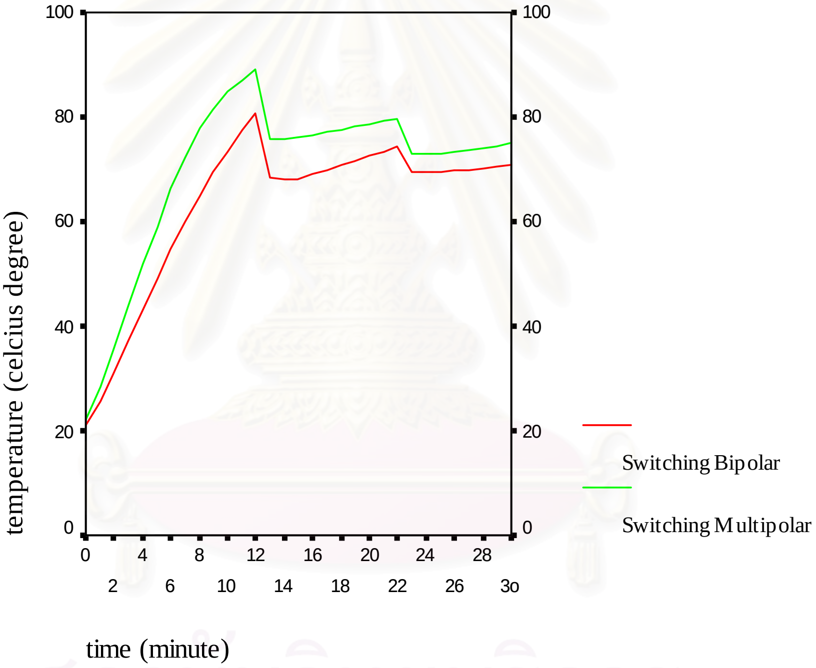

Figure 18. Graphs of mean temperature at the center portion of the triangle that connected each electrode in each group.

Furthermore, in the switching multipolar group, the current and power output were gradually increased during RF ablation in all sessions. The mean current flow in switching multipolar and switching bipolar groups were 2.30 ± 0.17 A and 1.76 ± 0.23 A, respectively (p < 0.001). Value of voltage output was an inverse proportion by the current. The mean voltage output for each group was as follows: 83.85 ± 3.27 volt in switching multipolar group and 88.75 ± 1.05 volt in switching bipolar group (p < 0.001). In addition, the mean power output for each group was as follows: 96.18 ± 3.44 % in switching multipolar group and 77.45 ± 10.07 % in switching bipolar group (p < 0.001) In comparison of each group, the differences in mean current, voltage output and power output between switching multipolar and switching bipolar groups were statistically significant. The current, voltage output and power output in each session were shown in table 4. The graphs in figure 19, 20, and 21 show the mean current, voltage output and power output in all three sessions, respectively.

Table 3. The initial and final temperatures in each session of the two groups

	Switching Multipolar	**Switching bipolar**	**P value**
1st session			
Initial temperature(°C)	28.56 ± 1.86	25.56 ± 2.11	0.027
Final temperature (°C)	89.16 ± 9.81	80.76 ± 13.69	0.016
2nd session			
Initial temperature(°C)	75.68 ± 7.17	68.32 ± 7.47	0.001
Final temperature(°C)	79.72 ± 7.75	74.40 ± 10.53	0.047
3rd session			
Initial temperature(°C)	73.00 ± 6.47	69.52 ± 8.38	0.107
Final temperature(°C)	74.92 ± 7.41	70.92 ± 8.82	0.089

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Table 4. The current, voltage output and power output in each session of the two groups

	Switching Multipolar	**Switching bipolar**	**P value**
1st session			
Current (A)	2.21 ± 0.23	1.60 ± 0.29	< 0.001
Voltage output (V)	85.20 ± 4.12	88.62 ± 2.45	0.001
Power output (%)	93.48 ± 5.73	71.09 ± 12.29	< 0.001
2nd session			
Current (A)	2.38 ± 0.25	1.89 ± 0.28	< 0.001
Voltage output (V)	82.89 ± 6.25	88.86 ± 1.11	< 0.001
Power output (%)	97.38 ± 3.82	83.04 ± 11.81	< 0.001
3rd session			
Current (A)	2.38 ± 0.19	1.83 ± 0.24	< 0.001
Voltage output (V)	82.71± 5.42	89.06 ± 0.80	< 0.001
Power output (%)	98.60 ± 3.71	79.74 ± 11.22	< 0.001

Note. A: Ampere, V: Volt.

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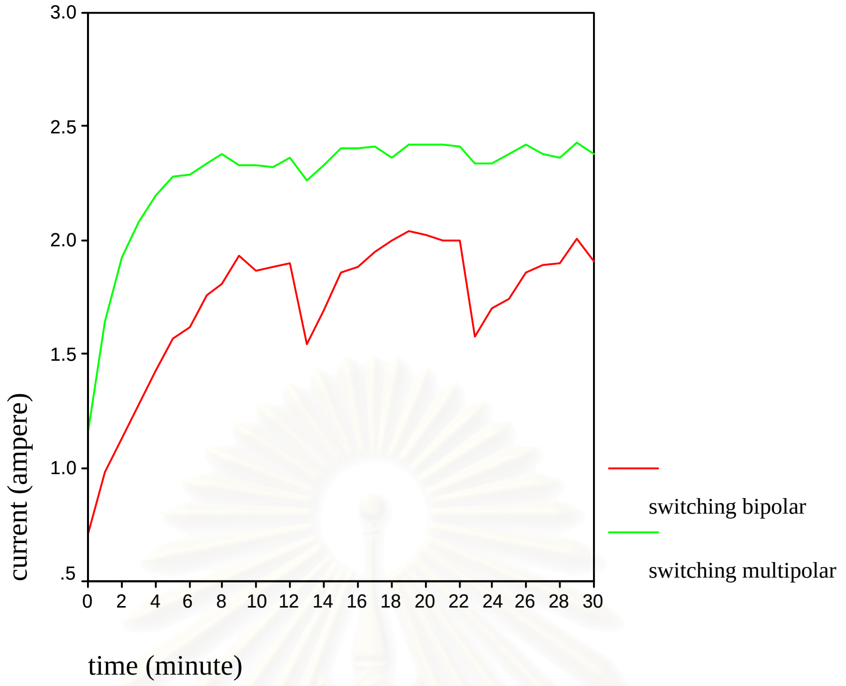

Figure 19. Graphs of mean current in each group. Note that higher current occurred with the switching multipolar group than with switching bipolar group.

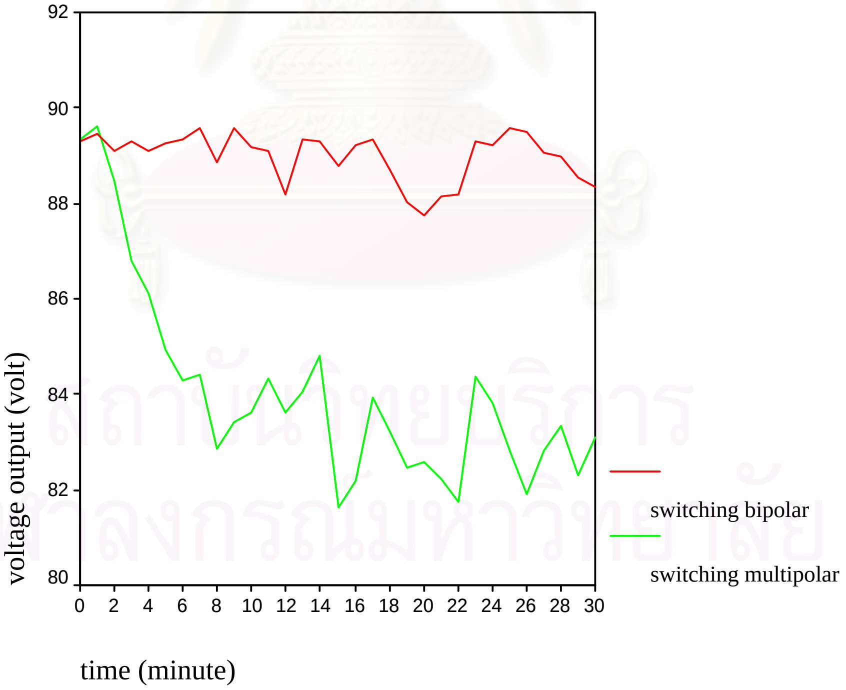

Figure 20. Graphs of mean voltage output in each group. Note that higher voltage output occurred with the switching bipolar group than with switching multipolar group.

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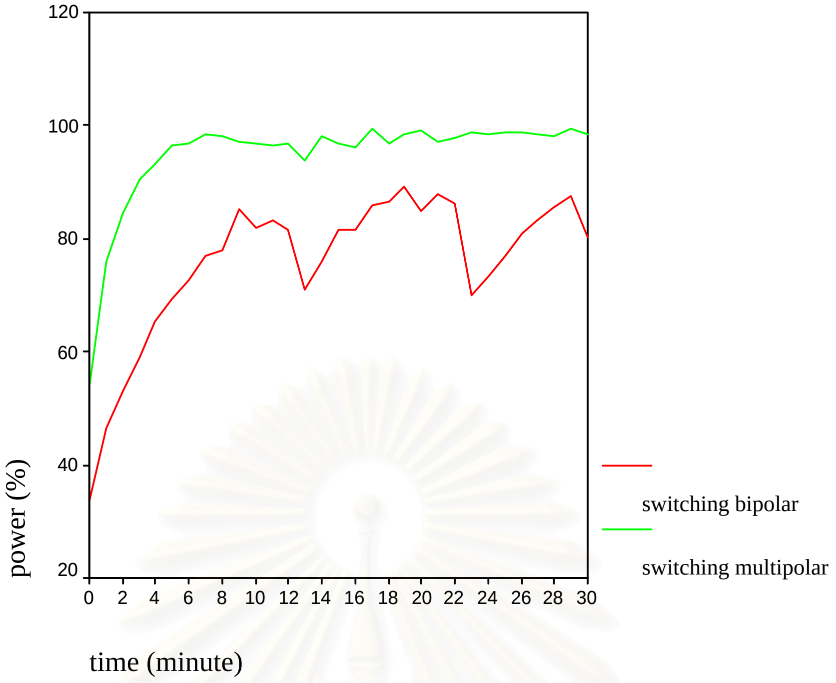

Figure 21. Graphs of mean power output in each group. Note that higher power output occurred with the switching multipolar group than with switching bipolar group.

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CHAPTER V
DISCUSSION AND CONCLUSION

Some recent studies have introduced the use of multiple RF electrodes as a strategy to increase the dimension of the spherically shaped ablation regions [26-34]. Multiple electrodes (two or more) can be utilized to deliver RF energy in several FRA modes: the consecutive monopolar, simultaneous monopolar, switching monopolar, switching bipolar and multipolar modes [12, 26, 32]. The consecutive mode applies energy continuously to one electrode and requires a long procedure time. The simultaneous mode is the synchronous application of energy to all electrodes. In this mode the maximal energy of any electrode is reduced in relation to the number of electrodes used (Ohm's law). In the switching monopolar mode, power is applied to only a single electrode at a time and there is no electrical interference between electrodes. All of the monopolar techniques required the grounding pad to complete the electrical circuit, so it is possible that patients could be at greater risk for skin burns. The switching bipolar mode with bipolar probes applies RF energy to one electrode and the other electrode is used as a return electrode, like the bipolar mode, but all the possible electrode pairs of the multiple electrodes are activated for a short period of time [28]. In the multipolar mode, RF current is passed through one electrode and the other two electrodes are used as the return electrodes. In order to avoid the problem of a rapid rise in impedance during multipolar RFA, the investigators used hypertonic saline infusion during the RF energy delivery to decrease the rise in impedance by increasing the electrical and thermal conductivity [24]. Thus, the multipolar mode can correct disadvantages of the previous modes and can produce the large dimensions (Table 5).

In this study, we compared the efficiency of switching multipolar method with switching bipolar method to producing thermal coagulation lesion. The switching multipolar method was found better results for creating larger maximum diameter, vertical diameter and volume than the switching bipolar method. We suspect that the larger coagulation diameters and volume achieved with the switching multipolar method might be due to its better heat production efficiency at a given current level [26]. From the results in this study, values of the applied current and power output in the switching multipolar method were greater than the switching bipolar method. Thus, it caused the high energy deposition between the electrodes [31]. This large energy deposit with the switching multipolar technique may contribute to the creation of a large area of coagulation.

However, the values of minimum diameter in two groups were not different. The minimum diameter is an essential requirement for the therapy of primary and secondary liver tumors. If the minimum diameter of ablation lesion was shorter than the diameter of tumors, it was a greater risk for local recurrences [43]. In this study, the switching multipolar and switching bipolar methods were comparable in ability to create the minimum diameter. Moreover, the minimum diameter in this study was still larger than the previous studies (Table 5).

With these two switching methods, liver tissue was heated uniformly between electrodes. The thermal lesions resulting from the experiment showed the same spherical shaped ablation zone in both groups. Values of the isometric ratio were 1.18 ± 0.09 in switching multipolar group and 1.18 ± 0.15 in switching bipolar group (p = 0.963). This value indicated about the roundness of thermal lesion [26, 31]. Creating spherical ablation zones could be valuable in the clinical application of RFA for liver tumors as focal liver lesions are usually round or oval-shaped [26].

Furthermore, Haemmerich et al have demonstrated that an important benefit of switching method was the increased temperature created in the ablation lesion [32]. The average final temperature at the thermal lesion center was 74.92 ± 7.41°C for the switching multipolar method compared with 70.92 ± 8.82 °C for the switching bipolar method. Multiple electrodes ablation lesions were hot in the region between closely placed electrodes because of both the increased power deposition, and the thermal shielding effect of electrodes from vascular mediated cooling. Multiple electrodes could be arrayed around large vessels to overcome vascular cooling and increase the effectiveness of perivascular ablation, which may decrease local recurrence of the primary and secondary liver tumors.

However, switching electrodes at fixed time intervals was less efficient than using an impedance-controlled algorithm [34]. Laeseke et al have demonstrated that switching the electrode at a shorter time than that required to cause an impedance spike may lead to allow intact perfusion to cool the tissue close to this electrode while the other electrodes were activated. Therefore, this tissue would have to be reheated during the next cycle of power application. On the other hand, longer time intervals may be more effective in creating vascular thrombosis but only minimal power could be delivered. However, in this study, the RF generator can not deliver the power with an impedance-controlled algorithm so we use the switching electrodes at fixed time interval method instead.

In our study, we performed three ablation sessions with the electrodes replacements to ensure that there was the effect on the shape and the overall volume of coagulation. The previous studies have demonstrated that bipolar method created non-spherical shaped ablation zone [20, 21]. Moreover, in multipolar method, the application of RF energy switched between electric fields that are parallel to the applicators and electric fields that cross the target tissue within the applicators [30]. Therefore, the three ablation sessions with the electrodes replacements not only compensate the irregular lesion with the single application but also increase the diameters and volume of the ablation lesion. Although, this method took a long time but it could produce a larger ablation volume than the methods in the previous studies (Table 6).

The switching multipolar technique and switching bipolar technique used in this study have several similarities, such as their use of multiple electrodes and switching the delivery of RF energy to some of the electrodes as well as the advantage of heat trapping between the electrodes. Not only that, they also do not require a grounding pad to complete the circuit. However, the disadvantages of these two methods include the necessity of precise electrode placement on each side of a targeted liver tissue. In addition, in these two RF modes, applied power can not be controlled independently for each electrode [26].

Our study has certain limitations. First, the experiments were performed with normal liver parenchyma ex vivo, not with liver tumor. A major restriction of ex vivo RF ablation is that perfusion mediated tissue cooling and heat sink effects are not taken into consideration [30]. Thus, the volume of coagulation will be reduced in vivo, and the shape could be altered by blood vessels [35]. Nevertheless, ex vivo experiments are important for the initial evaluation of new techniques of RF ablation. Second, the size of some porcine livers is too small to test the performance of our methods with the greatest possible degree of optimization. Considering that in this study, the vertical diameter of ablation lesions reached the maximum thickness of the liver (Fig. 22). Third, when using switching multipolar method, the electrodes must be placed equidistant from each other. If the electrodes are not precisely placed, the current could flow to the nearest portion of the ground electrode, resulting in an irregular shaped ablation lesion (Fig. 23).

The initial investigation of switching multipolar and switching bipolar RF ablations in the ex vivo porcine liver is limited by several factors. Further in vivo evaluation and improvement of this technique is necessary. We expect that the multiple electrodes ablation with the use of the switching multipolar method will result in greater thermal lesions than the switching bipolar method in the in vivo experiment, as has been observed in our study.

In conclusion, findings from our ex vivo study demonstrated that switching multipolar RFA shows better capability to create a large round zone of thermal coagulation than switching bipolar RFA. We believe that the increased diameters and volume of thermal coagulation created by this technique would be significant clinical benefit in the therapy of liver tumors.

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Table 5. The dimensions of the RF-induced ablation zones according to the RF power application modes

Author	Mode	Dmax (cm)	Dmin (cm)	Dv (cm)
Lee et al (2005)	Monopolar	7.2 ± 0.3	4.2 ± 0.6	4.1 ± 0.3
	Bipolar	6.7 ± 0.7	5.8 ± 0.9	5.4 ± 0.4
Haemmerich et al. (2005)	Monopolar			
	- sequential	7.3 ± 7	6.5 ± 6	4.8 ± 5
	- simultaneous	NA	NA	3.4 ± 7
	- rapid switching	6.8 ± 9	6.2 ± 8	4.6 ± 5
Lee et al. (2007)	Monopolar			
	- sequential	5.5 ± 0.2	5.3 ± 0.3	4.8 ± 0.6
	- switching	5.3 ± 0.3	5.0 ± 0.4	4.9 ± 0.1
Lee et al. (2006)	Monopolar			
	- sequential	2.7 ± 0.1	2.4 ± 0.2	3.8 ± 0.4
	- simultaneous	5.7 ± 0.7	3.5 ± 1.0	4.3 ± 0.3
	Multipolar	5.7 ± 0.5	5.2 ± 0.3	5.0 ± 0.4
Our study (2008)	Switching bipolar	8.12 ± 0.6	6.93 ± 0.6	4.22 ± 0.6
	Switching multipolar	8.54 ± 0.4	7.24 ± 0.5	4.81 ± 0.6

Note. Dmax: maximum diameter, Dmin: minimum diameter, Dv: vertical diameter, NA: not applicable.

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Table 6. The duration and volume of the RF-induced ablation zones according to the RF power application modes

Author	**Mode**	**Duration (minute)**	**Volume (cm^3)**
Lee et al. (2005)	Monopolar	20	65.7 ± 12.7
	Bipolar	20	111.6 ± 30
Lee et al. (2005)	Bipolar	20	107.6 ± 34
Haemmerich et al. (2005)	Monopolar		
	- Sequential	36	137.5 ± 22.2
	- Simultaneous	12	22.3 ± 6.4
	- Rapid switching	12	116.4 ± 15.2
Lee et al. (2007)	Monopolar		
	- Sequential	36	72.9 ± 12.6
	- Switching	12	65.7 ± 12.6
Clasen et al. (2006)	Multipolar	60	101 ± 39
Lee et al. (2006)	Monopolar		
	- sequential	36	37.6 ± 4.0
	- simultaneous	12	44.9 ± 12.7
	Multipolar	20	78.9 ± 6.9
Our study (2008)	Switching bipolar	30	125.49 ± 29.72
	Switching multipolar	30	156.51 ± 26.81

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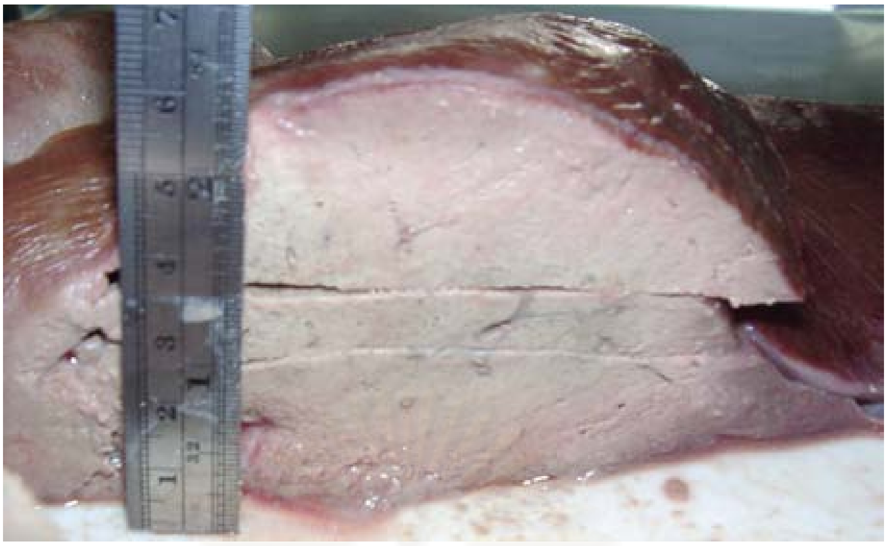

Figure 22. The vertical diameter of ablation lesions reached the maximum thickness of the liver.

Figure 23. An irregular shaped ablation lesion.

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APPENDICES

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APPENDIX A

Principles and Techniques of Radiofrequency Ablation

Radiofrequency (RF) ablation is a minimally invasive procedure that has emerged as the most powerful technique for tumor destruction and is nowadays established as the primary ablative modality at most institutions (Fig. 1).

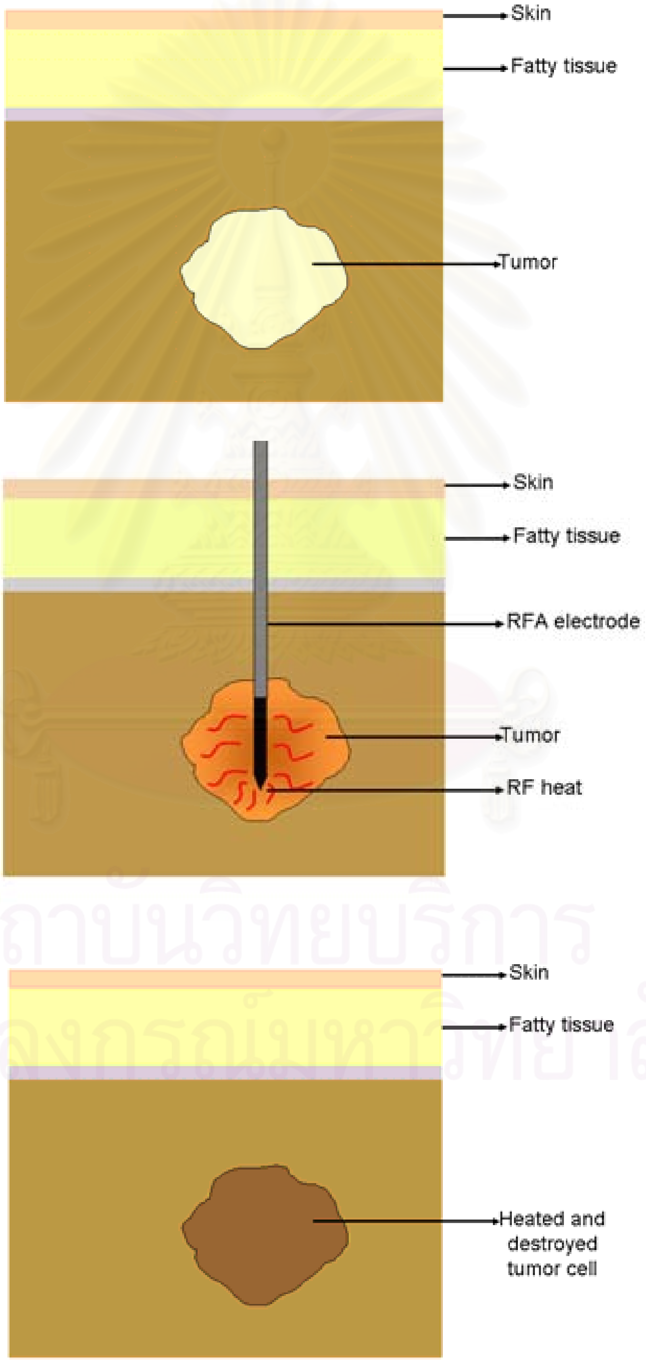

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Figure 1. Radiofrequency ablation.

1. Basic Principles

The goal of RF ablation is to induce thermal injury to the tissue through electromagnetic energy deposition. The term RF ablation applies to coagulation induced by all electromagnetic energy sources with frequencies less than 900 kHz, although most devices function in the range of 375–500 kHz. The term RF refers not to the emitted wave but rather to the alternating electric current that oscillates in this frequency range. In monopolar RF ablation (Fig. 2), the patient is part of a closed-loop circuit that includes an RF generator, an electrode needle, and a large dispersive electrode (grounding pads). An alternating electric field is created within the tissue of the patient (Fig. 3). Because of the relatively high electrical resistance of tissue in comparison with the metal electrodes, there is marked agitation of the ions present in the target tissue that surrounds the electrode, since the tissue ions attempt to follow the changes in direction of the alternating electric current. The agitation results in frictional heat around the electrode. The discrepancy between the small surface area of the needle electrode and the large area of the ground pads causes the generated heat to be focused and concentrated around the needle electrode.

The thermal damage caused by RF heating is dependent on both the tissue temperature achieved and the duration of heating (Fig. 4). Heating of tissue at 50–55°C for 4–6 min produces irreversible cellular damage. At temperatures between 60°C and 100°C near immediate protein coagulation is induced, with irreversible damage to mitochondrial and cytosolic enzymes as well as nucleic acid-histone protein complexes. Cells experiencing this extent of thermal damage most often, but not always, undergo coagulative necrosis over the course of several days. In fact, the zone of coagulation, while predominantly comprising coagulative necrosis, often lacks the classic well-defined histologic appearance of coagulative necrosis in the acute postablation period or even within some zones of adequately ablated tissue for many months after ablation. Indeed, in many cases, specialized stains are required to confirm that cellular death has been achieved after thermal ablation.

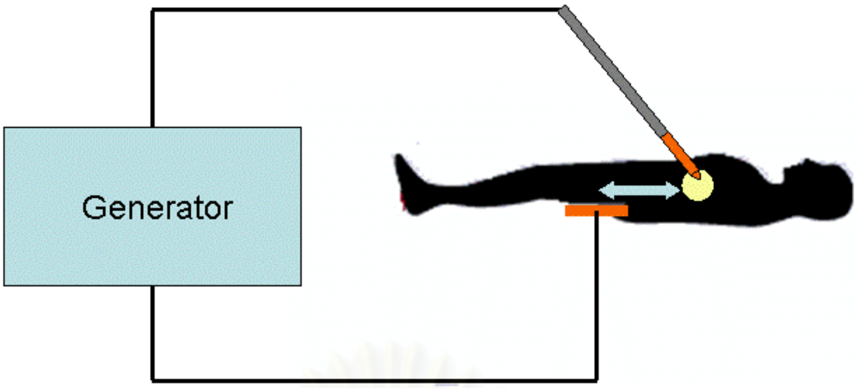

Figure 2. Monopolar RF ablation circuit.

For this reason and because many tumors undergo central necrosis without ablation therapy, the term “coagulation” is preferred over the use of “necrosis” alone, because it denotes that the ablation intervention is actively leading to tumor destruction. The more generalized term “coagulation” is preferred over the term “coagulative necrosis” because the latter term has a well-defined meaning in the pathology literature, including the absence of visible nuclei within the dead cells.

At 110°C, tissue vaporizes and carbonizes. These processes usually retard optimal ablation due to a resultant decrease in energy transmission. For adequate destruction of tumor tissue, the entire target volume must be subjected to cytotoxic temperatures. Thus, an essential objective of ablative therapy is achievement and maintenance of a 50–100°C temperature throughout the entire target volume for at least 4–6 min. However, the relatively slow thermal conduction from the electrode surface through the tissues may increase the duration of application to 10–30 min. On the other hand, the tissue temperature should not be increased over these values to avoid carbonization around the tip of the electrode due to excessive heating.

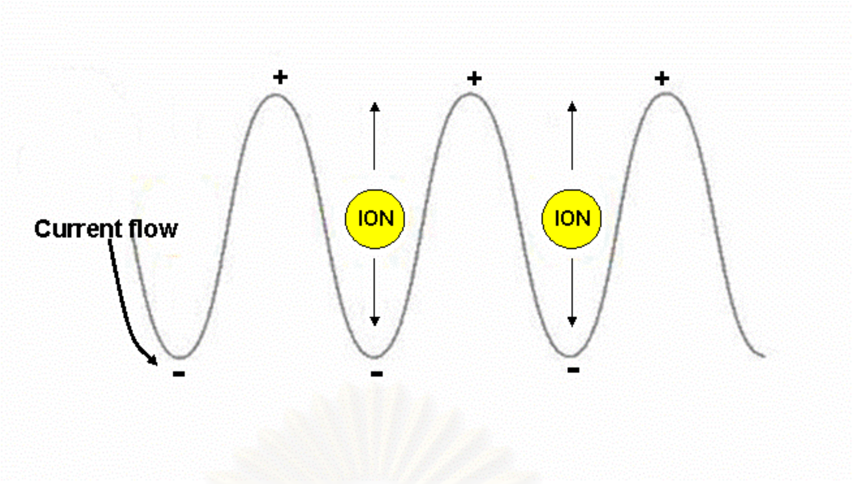

Figure 3. The alternating electric current. Schematic shows ionic agitation by alternating electric currents. The tissue ions are agitated as they attempt to follow the changes in direction of alternating electric current. The agitation results in frictional heat around the electrode.

2. Mechanisms of Energy Deposition

A major limitation of the technique is the small volume of ablation created by conventional monopolar electrodes. These devices are capable of producing cylindrical ablation zones not greater than 1.6 cm in the short axis. Therefore, multiple electrode insertions are necessary to treat all but the smallest lesions. Subsequently, several strategies for increasing the ablation zone achieved with RF treatment have been used. Heat efficacy is defined as the difference between the amount of heat produced and the amount of heat lost. Therefore, effective ablation can be achieved by optimizing heat production and minimizing heat loss within the area to be ablated. The relationship between these factors has been characterized as the “bio-heat equation.” The “bio-heat” equation governing RF-induced heat transfer through tissue as follows:

$$\text{Coagulation} = \text{energy deposited} \times \text{local tissue interactions} - \text{heat lost}$$

Heat production is correlated with the intensity and duration of the RF energy deposited. On the other hand, heat conduction or diffusion is usually explained as a factor of heat loss in regard to the electrode tip. Heat is lost mainly through convection by means of blood circulation.

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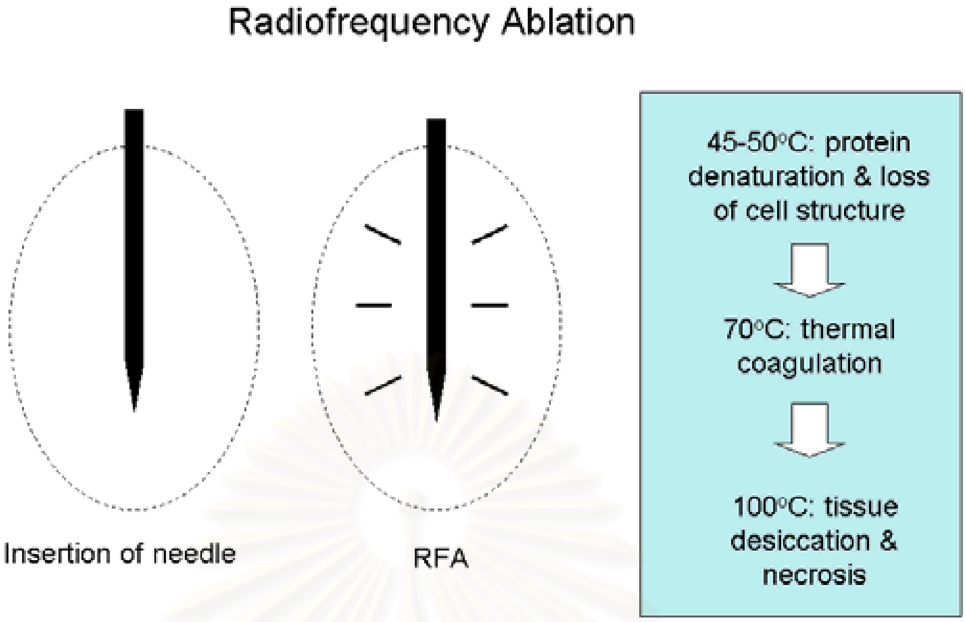

Figure 4. RFA causes ionic vibration, which leads to protein denaturation, thermal coagulation, and ultimately cell death.

3. Description of the instruments

The RF output of all commercially available generators has been increased to 150–200 W, which may potentially increase the intensity of the RF current deposited at the tissue. Major progress is achieved with the introduction of modified electrode needles, including internally cooled electrodes and multitined expandable electrodes with multiple retractable prongs on the tip. These techniques enable a substantial and reproducible enlargement of the ablation zone produced with a single needle insertion, and prompt the start of clinical application of RF ablation.

Internally cooled electrodes (Radionics®, Tyco Healthcare Group, Burlington, MA) consist of dual lumen electrodes with an exposed active tip of variable length (Fig. 5). Internal cooling is obtained by continuous perfusion with chilled saline and is aimed at preventing overheating of tissues nearest to the electrode to minimize carbonization and gas formation around the tip. The tip contains a thermocouple for recording the temperature of the adjacent tissue. To increase the size of the ablation, the company placed three of the cooled electrodes in a parallel triangular cluster with a common hub.

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Figure 5. Internally cooled and internally cooled cluster electrodes (Cool-tip® RF, Radionics®, Tyco Healthcare Group, Burlington, MA).

Multitined expandable electrodes have an active surface which can be substantially expanded by prongs deployed from the tip. The number of prongs and the length of their deployment vary according to the device and to the desired volume of ablation. The commercially available devices were developed to monitor the ablation process so that high-temperature coagulation may occur without exceeding a 110°C maximum temperature threshold. One device (RITA® Medical Systems, Mountain View, CA) relies on direct temperature measurement (Fig. 6). This kind of electrode, in fact, is made by an insulated outer cannula that houses nine curved electrodes of various lengths, which deploy out from the trocar tip. Five of the electrodes are hollow and contain thermocouples in their tips that are used to measure the tissue temperature. Probe-tip temperatures, tissue impedance, and wattage are displayed on the RF generator and are graphically recorded by dedicated software. Maximum power output of the RF generator, amount of electrode array deployment from the trocar, and duration of the effective time of the ablation (time at target temperature) depend on the desired volume of ablation. In fact, the generator runs by an automated program and maintains the target temperature throughout the procedure. At the end of the procedure, the coagulation of the needle track can be done after retraction of the hooks with the aim of preventing any tumor cell dissemination.

Another manufacturer (Radiotherapeutics® (Boston Scientific), Natick, MA) produces an RF ablation device that relies on electrical measurement of tissue impedance rather than on tissue temperature (Fig. 7). The electrode is made by an insulated 14-gauge outer needle that houses ten retractable curved electrodes. The electrodes are manufactured in different lengths. In application, the tip of the needle is advanced to the target tissue and the curved electrodes are deployed to full extension. The generator is switched on and energy is administered until a rapid rise in impedance occurs. The impedance of the tissue increases as the tissue desiccates. It is assumed that an ablation is successful if the device impedes out.

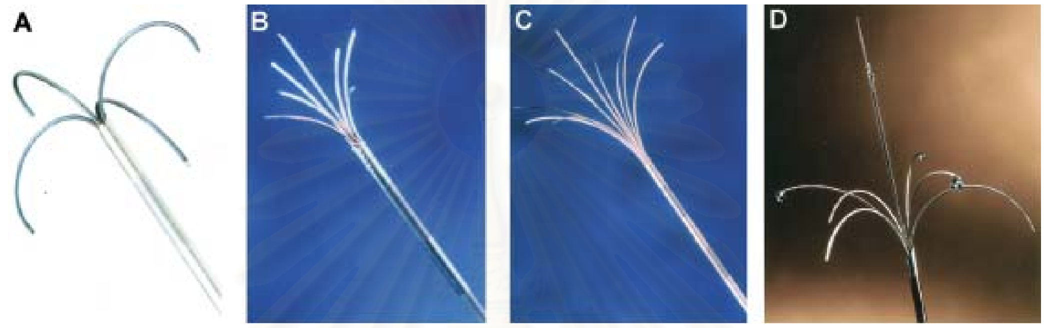

Figure 6. Multitined expandable electrodes (RITA® Medical Systems, Mountain View, CA). (A) RITA® Medical Systems model 30, (B) RITA® Medical Systems model 70, (C) RITA® Medical Systems model 90/StarBurst XL®, (D) RITA® Medical Systems model 100/StarBurst Xli® 70.

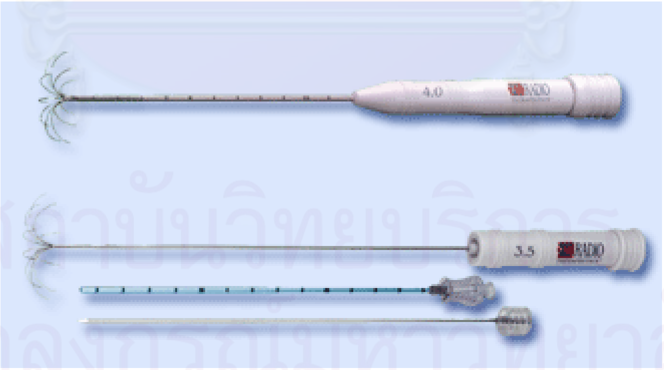

Figure 7. Multitined expandable electrodes (Radiotherapeutics® LeVeen® (Boston Scientific), Natick, MA).

The Berchtold® HiTT® (Fig. 8) hollow electrodes have one or more holes at the tip through which an isotonic or hypertonic saline solution at room temperature is infused into the tissue during RF coagulation. A fixed power is

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delivered by a 60W generator during a predetermined time, according to the desired coagulation diameter.

Figure 8. Berchtold® HiTT® 1-cm tip/1.2 mm diameter and 1.5-cm tip/2 mm diameter.

The Invatec® MIRAS® electrodes (Fig. 9) all have a bent thermistor that curves away from the tip to monitor tissue temperature. They are activated by a 100W generator. Each electrode has its own protocol. The MIRAS RC® is a unique type electrode with a coil that leaves the tip and is deployed perpendicularly to the shaft. The MIRAS LN® is an expandable electrode with four prongs that are deployed by pulling rather than by pushing. The MIRAS LC® is a flexible cooled-wet electrode. The MIRAS IOC® is a 6 mm diameter flexible cooled-wet electrode for intraoperative use.

Figure 9. Invatec® MIRAS RC®, MIRAS LN®, MIRAS LC®, MIRAS IOC® (from left to right).

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APPENDIX B

This thesis was a part of electrosurgical development which was financially supported by National Electronics and Computor Technology Center **(NECTEC)**, National Science and Technology Development Agency **(NSTDA)**.

NECTEC

a member of NSTDA

BIOGRAPHY

Miss Jutamart Pupud was born on April 5, 1983 in Songkhla, Thailand. She received her Bachelor degree of Science (Physical Therapy) with the second class honours in 2006 from the Department of Physical Therapy, Faculty of Allied Health Science**,** Chulalongkorn University, Bangkok, Thailand. She has enrolled in graduate program for Master degree of Medical Science at Faculty of Medicine, Chulalongkorn University since 2006.

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