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Intrahepatic Radiofrequency Ablation *Versus* Electrochemical Treatment *Ex Vivo*

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Background. **Radiofrequency ablation (RFA) and electrochemical treatment (ECT) are two methods of local liver tumor ablation. A reproducible perfusion model allowed us to compare these methods when applied in proximity to vascular structures.**

Material and Methods. **In a porcine liver perfusion model, we used RFA (group A) and ECT (group B) to perform ablations under ultrasound guidance within 10 mm of a vessel and examined the induced necrosis macroscopically and histologically.**

Results. **We created 83 lesions (RFA: 59, ECT: 24) in 27 livers. In group A (mean liver weight: 2046 g), perfusion was macroscopically found to limit necrosis in 52.5% of the procedures. Histology demonstrated the destruction of only 30.4% of the vessel walls within the ablation areas. In group B (mean liver weight: 1885 g), we detected reproducible and sharply demarcated ablation areas both macroscopically and histologically. Necrosis was unaffected by nearby vessels. No viable cells were found perivascularly. Histology showed destruction of the vascular endothelium without any discontinuities. We measured pH values of 0.9 (range: 0.6–1.8) at the anode and 12.2 (range: 11.4–12.6) at the cathode. Treatment time was 100 min when a charge of 300 coulombs was delivered.**

Conclusions. **Electrochemical treatment is a method of ablation that creates reproducible and predictable volumes of necrosis. It produces sharply demarcated areas of complete necrosis also in perivascular sites. ECT, however, requires much longer treatment times than RFA. In our model, the effects of RFA were considerably limited by perfusion, which caused incomplete areas of necrosis in proximity to vessels.**

Key Words: **electrochemical treatment; radiofrequency ablation; perfusion model; liver; necrosis; oncology; heat sink effect.**

INTRODUCTION

In many patients with malignant liver lesions, curative resection is no longer possible at the time of diagnosis [1–4]. Local ablative therapies such as radiofrequency ablation (RFA) or electrochemical treatment (ECT) are possible management options for these patients. RFA is a widely used thermal procedure that is reported to lead to incomplete tumor ablation in 0%–100% of treatment [2, 5], not in the least due to a cooling or heat sink effect from nearby vessels. ECT involves the placement of two or more electrodes into tissue and the continuous delivery of a direct current between the electrodes.

Following the groundbreaking work of Nordenstroem [6–9] around the year 1980, major clinical studies were conducted in China in the 1990s [10, 11]. Electrochemical treatment is reported to be associated with few complications and to effectively destroy tumor tissue. ECT causes ion and pH changes and thus induces coagulative and colliquative necrosis within the treated area. Since electrochemical treatment is a nonthermal procedure and is possibly unaffected by the heat sink effect from adjacent major vessels, which limits the effectiveness of radiofrequency ablation, ECT has conceivable advantages. Although basic research into the mechanisms underlying electrochemical treatment started as early as the 1970s, data available in the literature is limited and heterogeneous. For this reason, we

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used a reproducible porcine liver perfusion model to investigate and compare the effectiveness of RFA and ECT in terms of perivascular ablation.

MATERIAL AND METHODS

Porcine livers were obtained from a nearby commercial slaughterhouse. No animal was kept or killed for the purpose of this study. Since we used tissue specimens and not live animals, our study did not require approval under animal protection laws. Directly after the animals were killed, the livers were perfused through the portal vein and the hepatic artery with 10 L of a heparinized isotonic electrolyte solution (Ringer's solution with 2000 units of heparin per liter) at an organ temperature of 38.2°C (range 37.6–39.0°C).

The livers were then inserted into a perfusion system. The common hepatic artery was connected to a dialysis machine (Hospal Dasco BSM-22SC; Medolla, Italy), which was used to regulate arterial circulation (130 mmHg). A gear pump (ISMATEC ISM 405A; Glattbrugg, Switzerland) regulated portal venous circulation and provided a continuous flow (15–20 mmHg). During the experiments, the specimen was placed in a Plexiglas box and immersed in Ringer's solution to prevent its surface from drying out. The perfusate was passed through the vena cava and reached two gear pumps with two circulation thermostats (Haake, Type 001-4202/001-7992; Berlin, Germany; LKB 2219 Multitemp II, Bromme, Sweden), which provided coarse and fine temperature control. An oxygenator (Maquet, Jostra Quadrox Safeline; Hirrlingen, Germany) was used to enrich the temperature-controlled perfusate with oxygen.

In order to investigate electrochemical treatment, we used a direct current generator (ECU 300; Soering Medizintechnik, Quickborn, Germany) and platinum electrodes with a diameter of 1 mm.

The volume of necrosis that is induced by ECT depends on the applied electric charge, which is the product of electric current (in amperes) and time (in seconds) and is expressed in coulombs (C). One coulomb is defined as the quantity of electricity carried by a current of one ampere in one second ($1C = 1A \times 1s$). The electric current was ramped up to its preset level over a period of 5 s.

We performed our RFA experiments using a monopolar radiofrequency ablation system (RITA Medical Systems, Manchester, GA, model 1500X Generator, and a StarBurst Talon electrode array with a length of 25 cm and a diameter of 4 cm). In our study, the system delivered a maximum of 150 watts. The target electrode tip temperature was 105°C. Once the target temperature was reached, the treatment time was 10 min. At the end of the treatment episode, track ablation was performed at 25 watts for a further minute. To complete the electrical circuit, a metal grounding plate was placed into the Plexiglas box.

Under ultrasound guidance, RFA or ECT electrodes were inserted at a maximum distance of 10 mm from a vessel with a diameter of 5–7 mm and the ablation procedure was performed.

An Orion 3-Star Plus Portable pH Meter (Thermo Fisher Scientific, Waltham, MA) was used for measuring pH levels. The sensor had a diameter of 2 mm.

After initial fixation in buffered formalin, necrotic tissue specimens were stained according to a standard hematoxylin and eosin protocol and analyzed histologically at the Institute of Pathology of the University, Luebeck Medical School.

The χ^2, Fisher's exact test, and the Mann-Whitney U test were used for statistical analysis. Results were considered statistically significant at P value <0.05.

RESULTS

Radiofrequency Ablation

We inserted 15 organs with a mean weight of 2046 ± 707 g (range 1216–2544 g) into the perfusion model in order to investigate radiofrequency ablation in isolated perfused porcine livers. Mean post-interventional weight was 2107 + 645 g (range 1230–2636 g). This result shows that there was no significant increase in weight during the experiments ($P = 0.142$). The histologic examination revealed the absence of intracellular and interstitial edema in non-ablated liver tissue. Neither ECT nor RFA caused vascular thrombosis in the perfusion model.

In the 15 porcine livers, we performed a total of 59 radiofrequency ablations in close proximity to vessels. In 24 procedures, the umbrella-shaped RFA electrode array was fully deployed (level 5). Since the manufacturer's literature states that smaller liver lesions can be treated using a smaller array diameter, we performed a further 35 thermal ablations with the array partially retracted (level 3). The mean total duration of radiofrequency ablation, including the heating phase, the ablation procedure, and track ablation was 12.28 + 0.81 min (range 10.7–13.8 min) at level 3 and 12.43 + 1.17 min (range 11.8–15.5 min) at level 5 ($P = 0.433$). At level 5, the target temperature was not reached in 7 of 24 procedures (29.2%). When this was indicated by the RFA generator, the ablation procedure was discontinued. At level 3, all 35 procedures were successfully performed in the vicinity of vascular structures (Table 1).

TABLE 1

Macroscopic and Microscopic Analysis of 59 RFA-Induced Lesions

Heat sink effect	RFA (total)	RFA (level 3)	RFA (level 5)
Discontinuation (failure to reach target temperature)	11.9% (7 of 59)	0% (0 of 35)	29.2% (7 of 24)
Heat sink effect (macroscopic evidence)	52.5% (31 of 59)	42.9% (15 of 35)	66.7% (16 of 24)
Reduction in size	15.3% (9 of 59)	14.3% (5 of 35)	16.7% (4 of 24)
Incomplete ablation	20.3% (12 of 59)	17.1% (6 of 35)	25.0% (6 of 24)
Reduction in size and incomplete ablation	16.9% (10 of 59)	11.4% (4 of 35)	25.0% (6 of 24)
Heat sink effect (histologic evidence)			
Intact vessel walls (total necrosis)	70.1% (82 of 117)	69.6% (48 of 69)	70.8% (34 of 48)
Destroyed vessels (total necrosis)	29.9% (35 of 117)	30.4% (21 of 69)	29.2% (14 of 48)
Intact vessels within 1 cm from the electrode	57.8% (48 of 83)	56.3% (27 of 48)	60.0% (21 of 35)
Destroyed vessels within 1 cm from the electrode	42.2% (35 of 83)	43.8% (21 of 48)	40.0% (14 of 35)

Perivascular non-necrotic tissue portions and small-sized necrotic areas at the periphery were identified macroscopically.