Radiofrequency hepatic ablation with internally cooled electrodes and hybrid applicators with distant saline infusion using an in vivo porcine model

F. Burdí o a,*, A. Navarro b, E.J. Berjano c, J.M. Burdí o d, A. Gonzalez e, A. Güemes b, R. Sousa b, M. Rufas b, I. Cruz e, T. Castiella f, R. Lozano b, J.L. Lequerica g, L. Grande a

a Department of Surgery, Hospital del Mar, Barcelona, Spain
b Department of Surgery “A”, Hospital Clínico Universitario “Lozano Blesa”, Zaragoza, Spain
c Department of Electronic Engineering, Polytechnic University of Valencia, Valencia, Spain
d Department of Electric Engineering and Communications, University of Zaragoza, Zaragoza, Spain
e Department of Animal Pathology and Surgery, Veterinary Faculty, University of Zaragoza, Zaragoza, Spain
f Department of Pathology, Hospital Clínico Universitario “Lozano Blesa”, Zaragoza, Spain
g Instituto de Biomedicina de Valencia, CSIC, Valencia, Spain

Accepted 30 September 2007
Available online 26 November 2007

Abstract

Aims: Radiofrequency ablation (RFA) of tumors by means of internally cooled (ICE) or multitined expandable electrodes combined with infusion of saline into the tissue may improve results. Our aim was to determine the efficacy of a previously optimized hybrid ICE system (ICE combined with infusion of saline into the tissue at a distance of 2 mm) in comparison with a conventional ICE cluster electrode in porcine liver in vivo.

Methods: A total of 32 RFA were performed on a total of 10 farm pigs using two RFA systems: Group A (n = 16): Cluster electrode. Group B (n = 16): Hybrid system (with continuous infusion of 100 ml/h of 20% NaCl at 2 mm distance from the electrode shaft by an independent isolated needle). Livers were removed for macroscopic and histological assessment after the procedure. Coagulation volume, coagulation diameters, coefficient of variability (CV) of coagulation volume, sphericity ratio (SR), deposited power (DP), deposited energy (DE), deposited energy per coagulation volume (DEV) and rise of animal temperature during the procedure were compared and correlated among groups. Additionally, linear regression analysis was modeled to study the relationship between deposited energy and either coagulation volume and rise of animal temperature during the procedure in both groups.

Results: Both coagulation volume and short diameter of coagulation were significantly greater (p < 0.05) in group B compared to group A (22.7 ± 11.0 cm³ and 3.1 ± 0.7 cm vs. 13.5 ± 7.7 cm³ and 2.5 ± 0.5 cm, respectively). A similar CV and SR was observed among groups (57.1% and 1.4 ± 0.3 vs. 48.6% and 1.3 ± 0.2 for groups B and A, respectively). In group B, DE and DP were more than double group A, but DEV was nearly twice as high (9782 J/cm³ vs. 5342 J/cm³, for groups B and A, respectively). No significant relationship between DE and coagulation volume was encountered.

Conclusion: Efficacy of a single ICE may be improved with continuous infusion of saline at around 2 mm from the electrode shaft. Coagulation volume obtained with this improved system may be even greater than that obtained with a cluster electrode.

Keywords: Radiofrequency ablation; Liver tumors

Introduction

Since the time when radiofrequency ablation (RFA) was described as a local therapy capable of destroying liver malignancies, physicians have shown a great interest in this technique, as it could provide a minimal approach to treating many formerly untreatable patients. Early work with RFA was limited by the small ablation volumes that could be consistently achieved. The rapid increase of temperature (above 100 °C) at certain points of the tissue during RFA, leading to charring of the tissue and increase of impedance, was shown to be the main
determinant of these small coagulation volumes.\(^5,6\) Since then many strategies have been designed to improve deposition of energy into the tissue and further increase coagulation volumes, mainly using either multitined expandable or internally cooled electrodes (ICE), with similar effectiveness.\(^7,8\)

ICEs are largely employed in clinical practice, probably because they provide reliable geometry of coagulation zones\(^9,10\) while providing sufficient coagulation volume to treat medium or even large tumors (especially when using cluster electrodes\(^11\)). Conversely, perfusion electrodes (which allow infusion of saline through the active tip of the electrode into the tissue), even though they showed better efficiency in deposition of energy,\(^12–14\) demonstrated distortions of coagulation shape\(^9\) or an even higher rate of complications that have been linked to reflux of saline along the applicator path.\(^15,16\)

More recently, in order to safely enlarge the coagulation zone, a combination of systems has been employed in the same applicator. These hybrid systems (according to the terminology of The International Working Group of Image-Guided Tumor Ablation\(^17,18\)) usually combine the efficiency that stems from perfusion electrodes and the reliability of either a multitined electrode\(^5,19\) or ICE.\(^20,21\)

The benefit of combining saline perfusion into the tissue with ICE is an ongoing issue that is currently under evaluation. Two evidences published in medical literature have directed our research into this issue:

1. According to Goldberg et al.,\(^12\) perfusion of saline into the tissue may both improve conductivity of the tissue and transfer heat by convection in the hot spots during RFA.\(^12\) Better performance has been demonstrated with this technique, both in deposition of energy and volume of coagulation than the currently available technology either before\(^22\) or during RFA.\(^20,21,23–29\) Saline infusion has been injected into the tissue either through an aperture in the electrode itself\(^20,21,23–27\) or directly into the tissue.\(^22,28,29\)

2. Haemmerich et al.\(^30\) demonstrated that maximum temperatures were encountered about 2 mm away from the probe surface with conventional ICE.

Accordingly, we have recently demonstrated\(^31\) in ex vivo porcine liver that perfusion of saline into the tissue at around 2 mm from the electrode shaft while using an ICE improved deposition of energy and coagulation volume, compared to perfusion through the ICE itself (i.e., 0-mm perfusion distance) or beyond the hottest areas (i.e., 4-mm perfusion distance). In the present study we aimed to evaluate the efficacy of the former system of RFA in comparison with a conventional cluster ICE on in vivo porcine liver. Efficacy during ablation was evaluated by coagulation volume, short coagulation diameter and energy deposition.

Material and methods

In vivo experiments

A total of 32 RFA were performed on a total of 10 farm female adult pigs with a mean weight of 68 kg (range 61 to 78 kg) under general anesthesia. A 16-gauge silastic catheter (Drucafix Splittocan, Braun, Barcelona, Spain) was introduced through the internal jugular vein for central vein pressure and central temperature monitoring. Central temperature of the animal was tested both before the RF procedure and immediately after this procedure.

Each animal underwent a laparotomy and the liver was exposed. Four grounding pads were affixed to the back of the animal, as is current practice with cluster electrodes in the clinical setting. Two sets of 20-min RFA were performed using either: (1) Group A: Cluster electrode (\(n = 16\)) (Fig. 2) and (2) Group B: Simple ICE coupled with perfusion electrode—“the Hybrid system” (\(n = 16\)) (Fig. 3). In this group, continuous perfusion of saline was carried out at 2 mm from the ICE. In order to obtain enough perfused tissue for ablation, we performed all RFA near the dome of the liver, which is known to have higher blood perfusion\(^32\) and larger hepatic veins.\(^33\) This may be relevant since all thermal methods are negatively influenced by blood flow, which can dissipate heat during ablation.\(^17\) Given that neither blood perfusion\(^32\) nor size\(^33\) are homogeneous throughout the porcine hepatic lobes (i.e. lateral lobes are usually less perfused and smaller\(^33\)), each method was allocated alternatively through central and lateral lobes in each animal (Fig. 1). Only one RFA was performed on each liver lobe.

Figure 1. Schematic view of lobar anatomy of pig liver employed in the study: four lobes are described (left lateral lobe, left medial lobe, right medial lobe and right lateral lobe). White circles represent number of radiofrequency ablations. Hepatic veins are also depicted. All the ablations were performed near the dome of the liver. In each pig liver four RFA was performed (one in each lobe). Each method (cluster electrode and hybrid method) was allocated alternatively among central and lateral lobes (See text). Inside the circles are written the number of the thermal ablations performed in this study. Pig anatomy is based on Thein et al.\(^32\)
Experiments were conducted with a 480-kHz generator (model CC-1; Radionics, Burlington, MA, USA). In group A, Cluster electrodes (Cool-tip: Valleylab, Boulder, CO, USA) (Fig. 2) with 2.5 cm exposed tips were employed. In group B, simple 17-gauge ICEs with 3 cm exposed tips (Cool-tip; Valleylab) were used (Fig. 3). Perfusion of saline into the tissue (20% NaCl) at 100 ml/h at room temperature was performed by a pump (Alaris IPX1, Alaris Medical Systems, Basingstoke, UK). Saline perfusion was injected through an independent 14-gauge insulated needle assembled parallel by means of a metallic outer sheath and a fixation system attached to a simple 17-gauge ICE with 3 cm of exposed tip, similarly to Burdio et al.31 In both groups, a peristaltic pump (Watson Marlow, Wilmington, MA, USA) was used to deliver 0°C saline through the ICEs at 10–25 ml/min.

For all experiments, internal cooling of the electrode and perfusion of saline were begun before power deposition. The generator was set manually at 50, 100 W and maximum power at first, second and beyond third minute, respectively, similarly to Lee et al.20 and Kim et al. 21 Although the pulsed algorithm of power has been demonstrated to improve coagulation volume and deposited power,34 it probably reduces the risk of charring the tissue. In our study this algorithm was never employed to better recognize charring and easily identify rises of impedance. Nonetheless, radiofrequency delivery was interrupted for 1 min without interrupting either perfusion of saline or internal cooling, if a spontaneous rise of impedance over 200 Ω was observed (i.e. roll-off). The same power was then reapplied.

Assessment of coagulation necrosis and coagulation shape

In all cases, animals were euthanized by exsanguination immediately after the RFA procedures. Livers were then sectioned along the longitudinal and transverse axes of the “white zone” of coagulation necrosis (i.e. “red zone” was excluded from measurements). The “white zone” is generally accepted as coagulation necrosis.17 However, any doubtful coagulation zones were submitted to histopathologic analysis. Specimens were then fixed in formalin, paraffin embedded, cut and stained with Hematoxylin and Eosin. Three diameters were measured in each RFA by consensus of two observers: diameter along the applicator track (i.e. a-diameter or axial diameter) and both diameters (i.e., transverse diameters) perpendicular to the applicator axis (i.e. b- and c-diameters). Volume (V) was then calculated (V = (1/6)πabc). In all cases, the short diameter of the lesion was identified. The presence of charred tissue was also specifically assessed along the longitudinal axis of coagulation, next to the applicator, where it is known to be most frequently located with conventional ICEs.30 Charred
tissue was defined, similarly to McGahan et al., as any dark tissue usually near the electrode path surrounded by a pale or white coagulation zone.

Coagulation shape was assessed by the sphericity ratio (SR). This ratio was defined as the fraction produced by the largest and the average of the two remaining diameters in each lesion. The closer this ratio is to 1, the more spherical the shape. Additionally, as a measure of reproducibility we calculated the coefficient of variability (CV) of the coagulation volume, which had previously been defined as the ratio between standard deviation of volume size and mean value of volume for each group, expressed as a percentage.

Statistical analysis

Continuous variables were compared and correlated among groups. A Kolmogorov-Smirnov test was used to determine whether values followed a normal distribution. Student’s t-test and the Mann-Whitney U-test were used to analyze mean values. Linear regression analysis was also modeled to study deposited energy. In this regard, coefficient of determination \( r^2 \) was provided when any significance was detected. Statistical analyses were performed with SPSS version 12.0 (SPSS, Chicago, IL) statistical software.

Results

All the animals tolerated the experiment well, with minor variations in blood pressure. Thirty-two RFA were created in ten livers (See Fig. 1). Seven RFA of group A and 8 RFA of group B were performed in lateral lobes.

Assessment of coagulation volume, diameter and shape

In all cases the short diameter of coagulation necrosis was one of the two transverse diameters and the largest was the axial. No significant differences were encountered in the axial diameter between the groups. However, both transverse diameters were at least 20% greater on average in group B than in group A (Table 1). Therefore, an average of 60% increase in coagulation volume was observed in group B over group A. In group B the reproducibility of coagulation volume evaluated by CV was even better than in group A (see Table 1) even though perfusion of saline into the tissue was performed with the former method. Nevertheless, in spite of the differences in transverse diameters between the groups with similar axial diameters, there were no differences in SR (Table 1).

Gross and histological evaluation

In group A, a char tissue ring was always observed. In group B, in spite of using perfusion of saline into the tissue,
charring of the tissue was actually not avoided and several degrees of heterogeneous char tissue were encountered (Fig. 4). No collateral thermal damage to close structures was detected. Histologic examination of selected specimens confirmed the presence of coagulation necrosis.

**Discussion**

**Rationale for distant infusion of saline during RFA with ICEs**

In RFA of the liver, Lorentzen demonstrated that a concentric ring of char tissue at about 3 mm from the needle tract was often observed during ablation with ICE and a non-pulsed power algorithm. Moreover, this charred tissue was linked to a significant fall in deposited power during ablation. This finding matched fairly well with the study by Haemmerich et al., who demonstrated that maximum temperatures were encountered about 2 mm away from the conventional ICE. On the other hand, Goldberg et al. stated that perfusion of saline may improve conductivity of the tissue and transfer heat by convection in the hot spots during RFA. Accordingly, we recently demonstrated in ex vivo porcine liver that perfusion of saline into the tissue at around 2 mm from the electrode shaft while using an

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Group A:</th>
<th>Group B:</th>
<th>( p^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cluster electrode</td>
<td>Hybrid system</td>
<td></td>
</tr>
<tr>
<td>Coagulation volume (cm(^3))</td>
<td>13.5 ± 7.7</td>
<td>22.7 ± 11.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Coefficient of variability(^a)</td>
<td>57.1%</td>
<td>48.6%</td>
<td>NS</td>
</tr>
<tr>
<td>Axial diameter (cm)</td>
<td>3.6 ± 0.4</td>
<td>4.1 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Minimum transverse diameter (cm)</td>
<td>2.5 ± 0.5</td>
<td>3.1 ± 0.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Maximum transverse diameter (cm)</td>
<td>2.6 ± 0.7</td>
<td>3.2 ± 0.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sphericity ratio(^b)</td>
<td>1.4 ± 0.3</td>
<td>1.3 ± 0.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

\( ^a \) Global statistical significance. The values were expressed as mean ± SD. Statistically significant (\( p < 0.05 \)). NS, no significant difference.

\( ^b \) Sphericity ratio was defined as the fraction of the largest and the average of the two remaining diameters in each lesion. The closer this ratio is to 1, the more spherical the shape.

**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Group A:</th>
<th>Group B:</th>
<th>( p^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cluster electrode</td>
<td>Hybrid system</td>
<td></td>
</tr>
<tr>
<td>Deposited power (W)</td>
<td>53.5 ± 18.0</td>
<td>135.5 ± 22.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deposited energy (J)</td>
<td>64158 ± 21602</td>
<td>163001 ± 27453</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deposited energy per lesion volume (J/cm(^3))(^a)</td>
<td>5342 ± 1616</td>
<td>9782 ± 7687</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Rise of animal temperature during the procedure (°C)</td>
<td>0.0 ± 0.2</td>
<td>0.6 ± 0.5</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

\( ^a \) Global statistical significance. Statistically significant (\( p < 0.05 \)).

\( ^a \) Total delivered energy per volume of achieved lesion size.
ICE improved deposition of energy and coagulation volume compared to perfusion either through the ICE itself or beyond the hottest areas. Therefore, in the present study we aimed to evaluate the efficacy of this hybrid system (group B) of RFA in comparison with a conventional cluster ICE (group A) in porcine liver in vivo (which has been demonstrated to be an effective and reliable method in RFA of liver tissue).

**Evaluation of coagulation volume, diameter and shape**

In our study we demonstrated a significant ($p < 0.05$) improvement in both coagulation volume and short diameter of coagulation with the hybrid system in comparison to the conventional cluster electrode ($22.7 \pm 11.0 \text{ cm}^3$ and $3.1 \pm 0.7 \text{ cm}$ vs. $13.5 \pm 7.7 \text{ cm}^3$ and $2.5 \pm 0.5 \text{ cm}$, respectively).
respectively). Interestingly, this improvement in coagulation volume and short diameter of coagulation was achieved with at least similar reproducibility in group B compared to group A (CV: 48.6% vs. 57.1%, respectively) and a similar coagulation shape (SR: 1.3 ± 0.2 vs. 1.4 ± 0.3, respectively).

Concerning conventional cluster electrodes, Pereira et al.4 in an in vivo pig liver model described a mean coagulation volume and a mean short diameter that were in fact greater (20.5 cm³ and 3.0 cm, respectively) than in our group A. These authors further described a CV of only 13% and a similar SR of 1.38 for the same electrode. De Baere et al.7 obtained a mean coagulation volume of 24 cm³ for this last electrode in a similar approach and mean short diameter of 3.4 cm with a CV of 31%. Conversely, Shock et al.39 in a more recent publication achieved a mean short diameter of only 2.4 cm and an adverse CV of 69% in a similar pig liver model, which showed greater similarity to the figures obtained in our group A in the present article. In our experimental model, to obtain enough perfused tissue for ablation we performed all the ablations near the dome of the liver, which is known to have higher blood perfusion32 and larger hepatic veins.33 This higher blood perfusion in the targeted tissue may account for the relatively lower coagulation volume and relatively lower reproducibility due to the known “heat sink effect” linked to the cooling effect of adjacent vessels.17 Furthermore, in our experimental model a pulsed power algorithm was not employed so as to be better able to recognize charring and easily identify rises of impedance. This algorithm has been demonstrated to improve volume coagulation and deposition of power34 and could explain part of the differences between our group A and the results previously published by Pereira et al.9 and De Baere et al.7

Regarding the hybrid ICE, Lee et al.20 employed a method with infusion of saline through the ICE itself (i.e. perfusion distance: 0 mm). These authors obtained a mean coagulation volume of 43.7 cm³, a mean short diameter of 3.4 cm and a CV of 40% in a pig liver model, which showed rather better results than the figures obtained in group B in the present article. Again, both the choice of a higher blood perfusion area for the RFA and the use of manual energy deposition in our experimental model may account for the differences between these authors’ results and our data. This could be true especially if we keep in mind that in a previous ex vivo study31 we demonstrated a thirty per cent increase in volume size when perfusing saline at 2 mm from the ICE (as in group B of the present study) compared to a distance of 0 mm (as in the study performed by Lee et al.20).

Evaluation of energy deposition

Evaluation of energy deposition provided valuable information on explaining some of the differences in coagulation volume between both methods. Thus, in group B deposition of energy and deposited power were more than twice as much as in group A, but deposited energy per volume in group B was nearly twice that of group A (9782 J/cm³ vs. 5342 J/cm³, respectively) and no significant relationship was found between amount of deposited energy and coagulation volume. Therefore, with the hybrid system with infusion of saline at 2 mm it was easy to keep a relatively higher mean deposited power (135 W for 20 min) but an increase in deposited power did not always guarantee higher coagulation volume (Fig. 5b). In this group the fairly good relationship (r² = 0.3, p < 0.05) between deposition of energy and rise of animal temperature during the procedure further explains the destination of at least some of this deposited energy. It is likely that infusion of saline focused on the hottest points during ablation with an ICE effectively improved the conductivity of this vulnerable area and transferred heat away into the tissue without reducing reproducibility. Conversely, when three parallel electrodes with no infusion of saline into the tissue (cluster electrode) were employed, smaller coagulation volume was achieved and relatively less mean power (53 W for 20 min) was deposited, but a good correlation between deposited power and coagulation volume was obtained (r² = 0.7, p < 0.001). Therefore, the efficacy of this latter system was likely dependent on the ability to deliver energy into the tissue and on passive thermal conduction, as Haemmerich also found.30

Limitations of the study

1. This was an in vivo study in healthy pig livers with a relatively high negative influence of blood perfusion. RFA of tumoral tissue with different electrical and mechanical properties may therefore yield substantially different data.
2. Precise perfusion of saline was performed by a perfusion needle held by means of two fixation systems attached to the electrode to guarantee the parallel position in the desired location. However, the distance between ICE and the tip of the infusion needle inside the tissue was not measured but may be modified with respiratory motion.
3. Reproducibility of coagulation volume was evaluated by the CV which had previously been employed by others.9,36 Nevertheless, other systems of evaluation of this key variable are advisable since this hybrid method employs infusion of saline into the tissue.
4. No collateral thermal damage to close structures were detected. However, with the provided experiences examination of long-term postoperative complications were not available.

Conclusion

Efficacy with a single ICE may be improved with continuous infusion of saline at around 2 mm from the
electrode shaft. Coagulation volume obtained with this improved system may be even greater than that obtained with a cluster electrode.

Acknowledgments

This study was supported by a grant for medical research from the Spanish Government (FIS/PI052498). We would also like to thank the R+D+i Linguistic Assistance Office at the Universidad Politécnica de Valencia for their help in revising this paper. The authors declare that they did not receive any funding from any company.

Conflict of interest

The authors have not received any funding from any company to perform this study. This study was supported only by a grant for medical research from Spanish Govern (FIS/PI052498).

References