

ULTRASOUND OVERESTIMATES THE AREA OF NECROSIS DURING RADIOFREQUENCY ABLATION IN PORCINE LIVERS

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ABSTRACT

Background: Ultrasound is the most common imaging modality used to guide electrode insertion and estimate the necrotic zone during radiofrequency ablation (RFA) of hepatic tumors. However, most investigators agree that ultrasound inaccurately predicts the necrotic zone after RFA despite the scarcity of experimental and clinical evidence.

Objective: We aimed to compare the necrotic diameter estimated from ultrasound during RFA with the actual gross diameter in ex vivo porcine livers.

Methods: An internally-cooled electrode with a 3 cm uninsulated tip (Cooltip Radiofrequency System, Valleylab) was used to perform RFA for 6 and 12 minutes in ex vivo porcine livers under ultrasound guidance. Maximum horizontal and longitudinal diameters of the gross ablation zones were compared with the diameters of the hyperechoic zone created on ultrasound during RFA.

Results: There was a trend for increased horizontal diameter for both ultrasound (RFA 6 mins = 3.8 ± 0.5 cm vs. RFA 12 mins = 5.1 ± 1.0 cm; $p = 0.079$) and grossly (RFA 6 mins = 2.7 ± 0.27 cm vs. RFA 12 mins = 3.1 ± 0.24 cm; $p = 0.068$) with increased RFA duration from 6 to 12 minutes, which was not observed for the longitudinal diameter. Ultrasound consistently overestimated the actual necrotic diameter by 1.3 ± 0.8 cm (range = 0.4 to 3.6 cm) ($p = 0.01$) whether RFA was performed for 6 (1.0 ± 0.3 cm) or 12 (1.8 ± 1.2 cm) minutes.

Conclusion: Ultrasound led to overestimation of the true size of ablation zones regardless of the duration of ablation. The slight increase in the discrepancy with increased RFA duration suggests that an increased hyperechoic zone with prolonged ablation will not necessarily mean a proportionate increase in actual necrotic diameter.

Keywords: Hepatocellular carcinoma, Radio frequency ablation (RFA), Ultrasound, porcine liver, liver treatment, hepatoma, HCC

INTRODUCTION

Radiofrequency ablation (RFA) is the most frequent local ablation therapy used in patients with primary and metastatic hepatic tumors not amenable to surgical resection. Selective tumor ablation is facilitated by the precise insertion of a radiofrequency probe into the target lesion under image guidance. Multiple imaging techniques (sonography, computed tomography, and magnetic resonance) can be used to guide the percutaneous placement of thermal energy applicators into the selected target. However, the most common imaging technique used for guidance during RFA is sonography.¹ This is largely due to the benefits of sonography which include the real time visualization of applicator placement, portability of the technology, nearly universal availability and low cost. However, sonography may result in occasional poor lesion visualization because of a lack of innate tissue conspicuity, or overlying bone or gas containing structures.²

The production of microbubbles in and surrounding the tumor being ablated during the course of conventional ultrasound-guided RFA of liver tumors has traditionally been taken as a rough estimate of the extent of tissue necrosis. However, despite one clinical study that showed that the extent of microbubble formation 5 minutes after RFA on conventional ultrasound correlated closely with the area of necrosis as depicted by contrast-enhanced ultrasound done 3-5 days after RFA,³ the correlation between microbubble formation and actual histologic necrosis has been less reliable with very few studies available in the literature.^{2,4} We therefore aimed to compare the necrotic diameters during ultrasound-guided RFA as depicted by the outermost extent of microbubble formation with actual gross necrotic dimensions in ex vivo porcine livers.

MATERIALS AND METHODS

RF Ablation System

An internally cooled RFA electrode (Cooltip Radiofrequency system, Valleylab, CO, USA) was

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used in the present study. This system consisted of a radiofrequency generator to produce a current of 480 kHz at a maximal power of 200 W, an RFA electrode with a single probe, a water-pumping machine, and return grounding pads. The single-probe electrode was 17 gauge and contained internal dual channels through which chilled water was pumped by a peristaltic pump. The resultant cooling effect around the electrode tip reduces charring of the surrounding tissue that might decrease tissue conductivity and block the radiofrequency current.^{2,4}

RF Ablation Technique

Eight (8) freshly excised porcine livers were obtained from a slaughterhouse. Livers weighed an average of 3 kg each. During the experiment, the porcine liver was placed on a metal plate connected to the grounding pads of the internally cooled radiofrequency system. Ablations were performed for 6 and 12 minutes. The experiment was repeated 5 times for each time group.

Imaging Examination

A radiologist supervised the determination of ablation size immediately post ablation using an ultrasound with a 3.5MHz transducer. The hyperechoic lesions which corresponds to microbubble formation were measured horizontally and longitudinally immediately after RFA. (Figure 1)

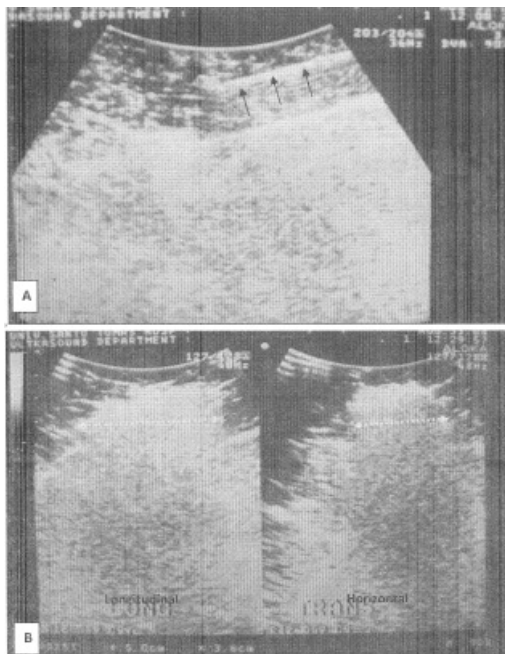


Fig 1.A. RFA Electrode (Arrows) Placement Under Real-Time Sonography, Pre-Ablation B. Measurement of the Hyperechoic Foci/Microbubble (dashed line) Post RF Ablation

Lesion Size Evaluation

Each ablation zone was then dissected along the plane perpendicular and parallel to the axis of the RFA electrode. Two observers working in consensus measured the white central area corresponding to the zone of coagulation necrosis using a clear plastic ruler. The maximum horizontal and longitudinal diameters were recorded.

Statistical Analysis

Statistical analysis was performed using independent t-test. Continuous variables were expressed as means ± SD with p values of less than 0.05 considered significant. All statistical analyses were performed using the SPSS v. 16 statistical package (SPSS, Inc., USA).

RESULTS

A total of 10 RFA lesions were created. The horizontal lesion diameters on ultrasound were significantly increased in the 12 minutes group when compared to the 6 minutes group, but with no significant difference in the longitudinal diameters (horizontal = 5.1±1.0cm [12 mins.] vs. 3.78±0.5cm [6 mins]; p = 0.039; longitudinal = 5.3±0.01cm [12 mins] vs. 5.1±0.3cm [6 mins]; p = 0.528). The same trend was observed when the gross necrotic diameters were analyzed, although the gross horizontal diameter did not reach statistical significance (horizontal = 3.05±0.2cm [12 mins.] vs, 2.68±0.3cm [6 mins]; p = 0.068; longitudinal = 4.3±0.6cm [12 mins.] vs. 4.1±0.2cm [6 mins]; p = 0.59). (Table I)

Table I. Mean Diameters of RF Induced Necrotic Zone Achieved Grossly and Sonographically At 6 and 12 Minutes Ablation.

	Ultrasound			Gross		
	6 minutes	12 minutes	p value	6 minutes	12 minutes	p value
Horizontal	3.78±0.49	5.1±1.04	0.039	2.68±0.27	3.05±0.24	0.068
Longitudinal	5.1±0.26	5.3±0.01	0.528	4.1±0.22	4.3±0.6	0.591

The measured horizontal and longitudinal gross necrotic diameters were significantly smaller than that measured on ultrasound (p, <0.05). The results did not differ whether the ablation was performed for 6 or 12 minutes. (Figure 2). Ultrasound consistently overestimated the actual horizontal necrotic diameter by 1.3±0.8cm (range = 0.4 to 3.6cm) The difference between the ultrasound and gross horizontal necrotic

diameter was significantly greater ($p = 0.024$) at 12 minutes ($2.1 \pm 1.2 \text{ cm}$) when compared to that at 6 minutes ($1.1 \pm 0.3 \text{ cm}$). However, the same cannot be concluded for the longitudinal diameter because despite a significant overestimation by ultrasound, there was no difference in the degree of overestimation when the RFA time was extended from 6 to 12 minutes (6 minutes = 0.9 ± 0.3 vs. 12 minutes = 1.0 ± 0.01 ; $p = 0.870$).

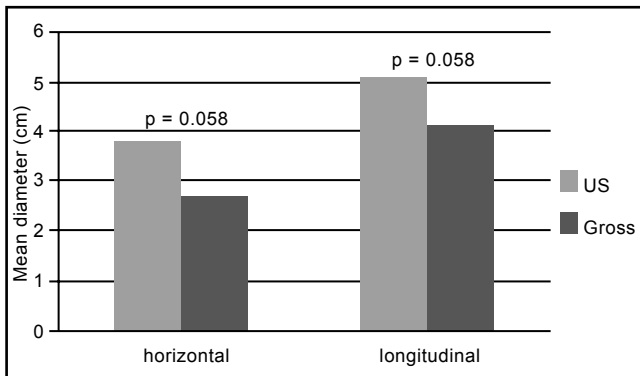


Fig 2A. Comparison of Ultrasound and Gross Necrotic Diameters at 6-Minute RF Ablation

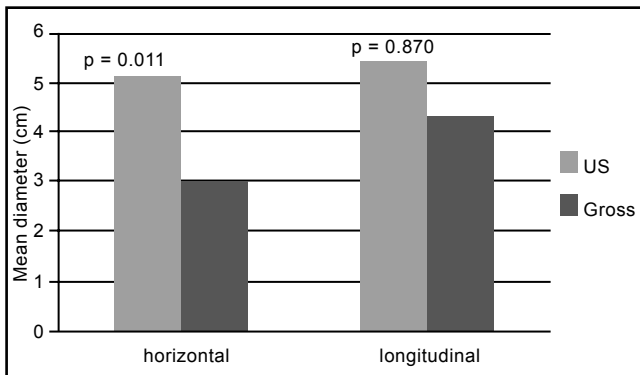


Fig 2B. Comparison of Ultrasound and Gross Necrotic Diameters at 12-Minute RF Ablation

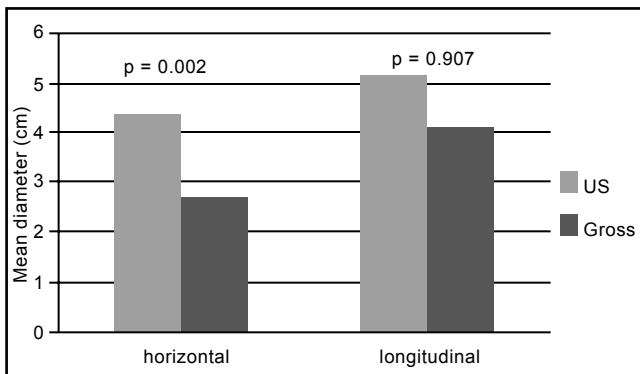


Fig 2C. Comparison of Ultrasound and Gross Necrotic Diameters Regardless of Duration of Ablation

DISCUSSION

Although ultrasound remains the most common imaging technique used to guide placement of the RFA electrode and to monitor the adequacy of ablation of the selected target, its accuracy in determining the extent of tissue coagulation induced by ablation still remains controversial. In our study, ultrasound consistently led to overestimation of the lesion size compared with the gross necrotic size. This is in contrast to results from earlier studies that have shown that ultrasound underestimates the actual necrotic area.^{2,4,5} There are fundamental differences between the earlier studies and ours. The most important of which is the actual “lesion” measured in ultrasound. Previous studies considered the hyperechoic zone formed by microbubble formation during ultrasound-guided RFA as mere artifacts and waited until these disappeared before using the mild differences in echogenicity at the liver to lesion interface as the borders of measurement. In contrast, our study considered the hyperechoic zone formed by microbubbles as the border of the RFA lesion. Although waiting for the microbubbles to subside may decrease the probability of overestimation of lesion size, there are inherent limitations to this technique as well. The most important of which is that RFA in these studies were performed in vivo in normal porcine livers.^{2,4} In actual patients with actual tumors, tumor echogenicity on ultrasound may vary widely from hypoechoic to hyperechoic to mixed echoic, and discernment of subtle changes in echogenicity induced by RFA may be easier said than done. Because of this, results may have very poor interobserver agreement and decrease the reliability of the technique.

The overestimation of the ablation zones in this study may be due to the inclusion of other artifacts, aside from microbubbles, created by thermal tissue changes during RFA. Our results concur with previous reports⁶⁻⁹ that the hyperechoic foci attributed to microbubble formation that increased in size during the procedure seen surrounding the distal portion of the electrode during radiofrequency energy application do not correspond to the area of tissue necrosis. The significant incremental increase in the ultrasound overestimation of the horizontal necrotic diameter from 6 to 12 minutes suggests that the reliability of measuring the extent of microbubble formation becomes worse the longer the RFA procedures becomes. Overestimation of the expected coagulation size may contribute to failure of local tumor control if interventional radiologists/hepatologists will rely solely on the areas where there was microbubble formation as an indication of the extent of ablation.

Although sonography is the most common modality used for real-time visualization of RFA electrode placement, clinical studies have shown the superiority of computed tomography (CT) in predicting the extent of coagulation necrosis.^{2,4,8,10} CT provides better identification of liver-lesion interfaces which is crucial in determining whether RFA has encompassed the whole tumor plus a 1 cm, ablative margin. Early identification of incomplete lesion necrosis means the treatment can be repeated and further ablation can be pursued. Moreover, earlier studies have shown better correlation of CT with lesion size on histopathology.^{2,4,5} However, the limitations of CT is that it is relatively expensive compared to ultrasound, and it is less portable which precludes its routine use.

The introduction of contrast enhanced ultrasound (CEUS) resolved these limitations of CT. it provided real-time guidance of needle positioning and monitoring of treatment. Extent of coagulation was better evaluated by CEUS, showing residual tumor foci immediately post-treatment, hence, further CEUS-guided re-treatment may be carried out.¹⁰ Initial experiences in CEUS detected presence of residual tissue with 100% sensitivity and 90% specificity.^{11,12}

CONCLUSION

Ultrasound led to overestimation of the true size of ablation zones regardless of the duration of ablation. The slight increase in the discrepancy with increased RFA duration suggests that an increased hyperechoic zone with prolonged ablation will not necessarily mean a proportionate increase in actual necrotic diameter. Overestimation of the expected coagulation size may contribute to failure of local tumor control if the microbubble formation will be used as an indication of the extent of ablation. Further investigations into the development of novel imaging strategies to enable rapid assessment of the extent of tissue destruction induced by RF ablation should be conducted.

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