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Gadolinium Augmentation of Myocardial Tissue Heating During Radiofrequency Ablation

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ABSTRACT

OBJECTIVES This study hypothesized that a metal already commonly used in medical procedures, gadolinium (Gd), will augment radiofrequency (RF) thermal injury and affect cardiac ablation lesions.

BACKGROUND Enhancement of RF ablation using metallic particles has been proposed for ablation of tumors.

METHODS A series of ablation lesions were delivered at variable power using an ex vivo model. Tissue temperatures and lesion characteristics were analyzed. Ablation in a porcine in vivo model after direct needle injection of the myocardium with Gd or after systemic administration of Gd encased in heat sensitive liposomes was also performed and compared to control values.

RESULTS Ablation after Gd infiltration of myocardial tissue resulted in significantly larger lesions at both low- and high-power settings. Larger impedance changes were observed during ablation of Gd-treated myocardium. In vivo ablation using a force-sensing irrigated tip catheter resulted in enhanced lesion sizes after Gd injection without a higher incidence of steam pops or perforation. Systemic administration of liposomal Gd with local release by RF heating did not result in larger ablation sizes.

CONCLUSIONS Gd can be used to enhance RF ablation lesions. In both ex vivo studies with a 4-mm ablation catheter under power control and in vivo findings with an irrigated tip catheter, ablation of myocardium infiltrated with Gd resulted in larger lesions, with altered RF electrical and thermal characteristics. More research is needed to refine the potential for Gd facilitation of RF ablation. The use of systemic heat-sensitive liposomes containing Gd with targeted release by RF heating did not affect lesion size. (J Am Coll Cardiol EP 2015;1:177–84) © 2015 by the American College of Cardiology Foundation.

Although radiofrequency (RF) ablation has revolutionized the treatment of cardiac arrhythmias, challenges remain in terms of efficacy and safety. The creation of durable lesions with RF energy for certain arrhythmias remains elusive. Pre-ablation treatment with an RF-facilitating agent may lead to enhanced electrical or thermal conductivity of targeted myocardial tissue and may improve outcomes (1). This strategy of using metals to augment ablation therapy is being actively explored in cancer therapeutics, with the use of gold, carbon, and palladium nanoparticles, among others (2–4). Cho et al. (3) showed that by functionalizing gold nanorods, they were able to locally target bladder cancer cells with thermal ablation. We chose to apply this similar concept for cardiac ablation therapy by considering the use of a metal—gadolinium (Gd)—that is already commonly used clinically in humans.

Chelated Gd is designed as a contrast agent for magnetic resonance imaging but it may have properties favorable for enhancement of RF-induced thermal injury of targeted myocardial tissue, similar to other metals. It is the only chelated metal approved by regulatory agencies for intravenous administration

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ABBREVIATIONS AND ACRONYMS

Gd = gadolinium

LV = left ventricle

RF = radiofrequency

and is an attractive candidate for use as an RF-facilitating agent in cardiac ablation.

In this study, we hypothesize that Gd can augment RF ablation and we sought to assess RF characteristics on myocardium after Gd infiltration in both the ex vivo and in vivo settings.

METHODS

EX VIVO MODEL. The experimental protocols have been approved by the Institutional Animal Care and Use Committees of the University of Colorado and University of Chicago. An ex vivo model was used, as previously described in detail elsewhere (5). Briefly, viable bovine myocardium was placed in a circulating saline bath at 37°C above a submersible load cell. The load cell was used to standardize application of energy by measuring force applied to the overlying myocardial tissue. Fluid was circulated in a saline bath at a rate of 5 l/min using a perfusion pump designed for cardiac bypass.

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DELIVERY OF RF ENERGY APPLIED TO INFILTRATED MYOCARDIUM. Using power control mode with a Stockert RF generator (Stockert, Freiburg, Germany) and a standard 4-mm ablation catheter (Celsius, Biosense-Webster, Diamond Bar, California), ablation at low power (20 W) and high power (50 W) was performed on recently excised, viable bovine myocardium. The catheter was mechanically fixed in a long deflectable sheath (Agilis, St. Jude Medical, Sunnyvale California) with precisely 10 g of force applied and with the catheter in a perpendicular position during RF delivery. Excised bovine myocardium specimens were approximately 5 cm × 7 cm in size. Multiple control and experimental lesions were placed on the same specimen; specimens from 10 animals were used. Immediately before RF energy delivery, the myocardium was infiltrated via direct needle injection to a depth of 5 mm, with 1 ml of Gd (Prohance) at a concentration of 279.3 mg/ml. Separate ablation lesions on the same myocardial tissue were produced using 2 types of control values: 1 ml of 0.9% saline injection (saline control), and needle insertion with no injection ("untreated control"). The number of lesions applied per ventricular section depended on the available endocardial surface. No lesions were placed over or in immediate proximity of papillary muscles (5 mm) or within immediate proximity of other lesions. Furthermore, no lesions were placed within 1 cm of section edge.

TISSUE TEMPERATURE ANALYSIS. T-type thermocouple wires were inserted horizontally into the myocardium at 3- and 5-mm depths and with the wire stem perpendicular to the ablation surface. Thermocouple analogue inputs were converted to digital signals using LabView software (version 7.0). Temperatures were recorded in a continuous fashion throughout the 60 s of RF application at a rate of 5 Hz. Peak tissue temperature was defined as the maximal temperature reading during RF application. RF applications that generated steam pops were excluded from temperature curve analysis.

IN VIVO EPICARDIAL AND ENDOCARDIAL ABLATION. Yorkshire pigs (n = 4) were anesthetized and intravenous lidocaine (50 to 100 mg) was used intraoperatively for prophylaxis of ventricular arrhythmias. The left ventricle (LV) was accessed using a retrograde aortic approach after femoral arterial access was obtained. Epicardial access was obtained in the same specimen under fluoroscopy using a 17-gauge Pajunk needle (Pajunk Medical Systems, Norcross, Georgia), and a 9-F sheath was placed in the epicardium. An electroanatomic map of the entire endocardium and epicardium was created using the CARTO3 mapping system (Biosense-Webster, Diamond Bar, California).

In 2 pigs, endocardial ablation was performed after direct injection of test substances as follows. Before ablation, 1 ml of either Gd (gadoteridol; ProHance) or 0.9% normal saline was injected to a depth of 5 mm into the myocardium using an endovascular mapping catheter with a retractable needle (Myostar, Biosense-Webster). The site and quality of injections were guided by fluoroscopy, intracardiac echocardiography, and the CARTO electroanatomic mapping system. Observation of premature ventricular complexes at the time of needle deployment and with expected morphology on the basis of site of ventricular contact helped to additionally confirm successful engagement of the needle with tissue. The needle/catheter position was recorded on the electroanatomical map at the time of injection. These markers were used to position the ablation catheter at the sites of injection. Caution was used to annotate catheter positions consistently during the same cardiac and respiratory cycle (end diastole and end expiration) to best verify that ablation was performed at sites of injection. Endocardial ablations were delivered at 50 W for 30 s with the same amount of force as measured by SmartTouch technology on the open irrigated tip RF catheters (Biosense-Webster); ablation lesions were tagged by the electroanatomic mapping system. The LV was divided into quadrants; ablations after Gd or control injections were performed in each

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