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Pre-Clinical Investigation of a Low-Intensity Collimated Ultrasound System for Pulmonary Vein Isolation in a Porcine Model

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ABSTRACT

OBJECTIVES The purpose of this study was to assess the feasibility of pulmonary vein (PV) isolation using low-intensity collimated ultrasound.

BACKGROUND Contemporary approaches to PV isolation are limited by the technical complexity of mapping and ablation. We describe a novel approach to left atrial anatomic rendering and PV isolation that aims to overcome some of these limitations by using low-intensity collimated ultrasound (LICU) system, which allows for near real-time geometry creation and automated ablation in a porcine model.

METHODS Twenty swine were anesthetized, and the LICU ablation catheter was placed in the left atrium via percutaneous transseptal access. Ultrasound M-mode–based anatomies of the inferior PVs were successfully created, and ablation was performed under automatic robotic control along a user-defined lesion path. One animal was excluded because of device failure.

RESULTS All target PVs in the 19 remaining animals were isolated acutely, requiring a mean of 1.6 applications. Ten animals were sacrificed acutely, and the remaining 9 survived for 35 ± 11 days. Of these 9, 1 animal was excluded from analysis because the index lasso position could not be reliably recreated. PVs in 5 of 8 animals remained isolated at sacrifice. Of the 77 total histological sections, 62 lesions (80.5%) were noted to be transmural. Lesions were homogeneous and characterized by coagulative necrosis and fibrous tissue. The mean myocardial thickness was 2.66 ± 1.80 mm, and the mean lesion depth was 4.28 ± 1.97 mm. No extra cardiac or collateral lesions were noted.

CONCLUSIONS This study demonstrates the safety and efficacy of a novel noncontact ultrasound mapping and ablation system to produce continuous transmural lesions that can isolate PVs in a porcine model. (J Am Coll Cardiol EP 2015;1:306–14) © 2015 by the American College of Cardiology Foundation.

Currently available approaches to pulmonary vein (PV) isolation can be broadly separated into 2 categories: 1) point-by-point ablation approaches that aim to create circular perivenous lesions that are, in aggregate, electrically isolating (1); and 2) single-application PV isolation approaches using either balloons or multipolar catheters (2-4). The success of the former approach depends on factors such as catheter tip design, contact force sensing capability, accurate left atrial (LA) and PV mapping, and, importantly, operator expertise in catheter manipulation (5,6). On the other hand, the single-application

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ablation approaches were designed to require somewhat less operator dependency to attain adequate expertise. However, these approaches are largely limited to isolation at the level of the PV ostia and with minimal effect on the PV antral regions and posterior LA (7). In light of these various limitations, it would be desirable to have a single integrated anatomic mapping and automated ablation system capable of creating uninterrupted transmural lesions along any user-defined path in the LA without these limitations.

To that end, we describe a novel approach to PV isolation that is capable of creating 1) near-real-time, noncontact 3-dimensional ultrasound anatomic renderings of the LA and PVs; followed by 2) robotically controlled perivenous ultrasound ablation. This technology aims to create continuous and transmural lesions along user-defined trajectories within the LA. In this preclinical study, we aim to assess the feasibility of this technology to achieve acute and chronic PV isolation followed by physiologic and histological assessment.

METHODS

The experimental protocol was approved by the respective institutional animal care and use committees at Mt. Sinai Hospital in New York, New York; University of Alabama at Birmingham, Alabama; and Sutter Institute for Medical Research in Sacramento, California. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

LOW-INTENSITY COLLIMATED ULTRASOUND SYSTEM. The low-intensity collimated ultrasound ablation system (LICU) (VytronUS, Inc., Sunnyvale, California) comprises the following major components: 1) a deflectable trans-septal sheath; 2) a robotic tip open-irrigated catheter with an additional manually deflectable section; and 3) an electronic control console (**Figure 1A**). The deflectable sheath is 13-F and capable of 135° of deflection. The distal tip of the catheter contains the proprietary LICU ultrasound transducer that is driven at approximately 10 MHz. The design of the transducer allows for creation of a highly collimated ultrasound beam. Thus the acoustic intensity (energy density) is effectively constant throughout the length of the beam from the face of the transducer to the maximum therapeutic range of 17 mm. The choice of frequency is such that blood is largely “transparent” to the beam with negligible ultrasound attenuation in the blood pool. The maximum therapeutic and imaging ranges of the ultrasound beam are 17 mm and 40 mm, respectively (**Figure 1B**).

The system produces endocardial geometry by robotically scanning the LA and PVs with the ultrasound-equipped catheter tip. A proprietary edge detection algorithm identifies the endocardial surface in individual M-mode lines; this range is then combined with tip position coordinate data to construct 2- and 3-dimensional maps of the chamber (**Figures 2A and 2B**). The anatomic map is superimposed with a color-coded range map that displays those sections that are within therapeutic ablation range of the transducer (purple, blue, green) and those that are beyond therapeutic range (yellow, orange, red). On this 2-dimensional mapped anatomy, the user then describes free-form lesion trajectories that are automatically ablated under robotic control without the need for continuous operator manipulation. The catheter is positioned in such a manner that the robotic movement of the catheter along the trajectory is uninterrupted. The interaction with the LA walls can be detected fluoroscopically or by interruptions during the smooth continuous creation of the anatomy. As described previously, the color-coded range map allows identification of regions of interest that are within the therapeutic range.

Because the maps and lesion trajectories are all self-referencing and nearly real time, they are minimally sensitive to external spatial error introduced by cardiac motion or fluid intake, among others. An approximately constant ultrasound beam speed at the endocardial surface is achieved by first scanning the target tissue along the desired trajectory to map the endocardial topography, and then using these data to robotically control the catheter tip’s velocity. The highly directional ultrasound beam generates thermal injury by absorption and dissipation of ultrasound energy as sound waves propagate through the target tissue. Because of the negligible dissipation of ultrasound energy in blood, lesion formation is relatively insensitive to the distance from the catheter tip to the target tissue.

The endocardial surface is cooled by both circulating blood in the LA and the saline infused through the catheter tip during ablation. The flow rate during mapping is 2 ml/min and during ablation is 15 ml/min. The LICU beam produces an acoustic radiation pressure that induces a jet of fluid in the direction of the beam. These mechanisms aim to prevent the formation of char or thrombus.

ABLATION PROCEDURE. After an overnight fast, 20 swine (mean weight, 74 kg) were pre-medicated,

ABBREVIATIONS AND ACRONYMS

HIFU = high-intensity focused ultrasound

ICPV = inferior common pulmonary vein

LA = left atrial

LICU = low-intensity collimated ultrasound ablation system

PV = pulmonary vein