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● *Original Contribution*

ULTRASOUND-GUIDED TRANSESOPHAGEAL HIGH-INTENSITY FOCUSED ULTRASOUND CARDIAC ABLATION IN A BEATING HEART: A PILOT FEASIBILITY STUDY IN PIGS

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Abstract—Catheter ablation for the treatment of arrhythmia is associated with significant complications and often-repeated procedures. Consequently, a less invasive and more efficient technique is required. Because high-intensity focused ultrasound (HIFU) enables the generation of precise thermal ablations in deep-seated tissues without harming the tissues in the propagation path, it has the potential to be used as a new ablation technique. A system capable of delivering HIFU into the heart by a transesophageal route using ultrasound (US) imaging guidance was developed and tested *in vivo* in six male pigs. HIFU exposures were performed on atria and ventricles. At the time of autopsy, visual inspection identified thermal lesions in the targeted areas in three of the animals. These lesions were confirmed by histologic analysis (mean size: 5.5 mm^2 × 11 mm^2). No esophageal thermal injury was observed. One animal presented with bradycardia due to an atrio-ventricular block, which provides real-time confirmation of an interaction between HIFU and the electrical circuits of the heart. Thus, US-guided HIFU has the potential to minimally invasively create myocardial lesions without an intra-cardiac device. (E-mail: francis.bessiere@inserm.fr) **© 2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **High-intensity focused ultrasound, Transesophageal ablation, Atrial fibrillation, Ventricular tachycardia, Minimally invasive ablation strategy, Ablation, Cardiac arrhythmia.**

INTRODUCTION

Catheter ablations for treating atrial fibrillation (AF) or ventricular tachycardia (VT) are complex procedures. Adverse events occur in 6% of AF ablations (Shah et al. 2012) and between 2% and 10% of VT ablations (Calkins et al. 2000; Reddy et al. 2003; Soejima et al. 2001; Wilber et al. 1995). The success rate for VT ablation is approximately 40% (Mallidi et al. 2011), and long-term (3 y) sinus rhythm is only maintained in 50% of AF ablations (Ganesan et al. 2013). Obtaining perfect electric isolation with cryo and radiofrequency catheters remains challenging due to difficulties in properly positioning the energy sources directly in contact with the cardiac walls (Cesario et al. 2007; Reddy et al. 2012). A less invasive method with more efficient energy and easier access is therefore potentially needed for complex procedures.

Because high-intensity focused ultrasound (HIFU) enables the generation of precise thermal ablations in deep-seated tissues while preserving adjacent and intervening tissues, it has the potential to be used as a new ablation technique for the heart. HIFU energy has already been used to create thermal lesions in cardiac tissues; specifically, two devices have been developed for AF treatment. The steerable HIFU balloon catheter (Prorhythm Inc., Ronkonkoma, NY, USA) creates circumferential lesions around pulmonary veins (Schmidt et al. 2007) using an endocardial method. Unfortunately, due to reports on the occurrence of atrioesophageal fistula, the HIFU balloon is no longer used in clinical practice (Borchert et al. 2008). The Epicor Medical Cardiac Ablation System (Saint Jude Medical, St. Paul, MN, USA) generates linear lesions on the left atrium using a surgical epicardial method (Mitnovetski et al. 2009; Ninet et al. 2005; Schopka et al. 2010). However, this invasive device was only useful in the treatment of AF that could be treated less invasively by an endovascular approach, and the company has stopped the production of this system. The feasibility of a transesophageal method using HIFU

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energy has been considered more recently (Hotaik et al. 2010; Pichardo and Hynynen 2007; Pichardo and Hynynen 2009; Werner et al. 2010; Yin et al. 2006). In humans, the esophagus is located just behind the heart and offers an excellent acoustic window for transesophageal echocardiography. Some targeted areas are located just in contact with the anterior face of the esophagus (left atrium) or are easily accessible with a left rotation or a trans-gastric positioning (left ventricle). During the same endoscopic procedure, dynamic focusing of the HIFU beam from the esophagus could allow for targeting both heart regions that are usually accessible with epicardial approaches and those that are usually treated with endocardial approaches. Moreover, the mid-myocardium of the ventricles could also be targeted. An endoesophageal HIFU device allows for focusing the ultrasound beam from the esophagus in such a way that the potential energy remaining after the focal point would be dissipated by the blood flow inside the heart cavities. Just as during transrectal HIFU procedures for treating prostate cancers and during the propagation of ultrasound through the rectal wall (Chapelon et al. 1999), cooling the endoesophageal probe protects the esophagus from thermal damage. The risk of deleterious effects is reduced compared to the HIFU balloon catheter that delivers energy from the heart outward. Ultrasound (US) imaging has been proposed to guide HIFU treatments using various approaches (endocavitary, intra-operative, and extracorporeal) and has shown promise in various organs at preclinical and clinical levels (Crouzet et al. 2010; Dupré et al. 2015; Illing et al. 2005; Ribault et al. 1998; Uchida et al. 2009; Vaezy et al. 2001; Wu et al. 2007). In the present work, guidance is defined as a method for positioning the HIFU source with respect to the target.

An endoesophageal HIFU probe that, for the first time, includes an on-board US imaging system optimized for real-time treatment planning and guidance in the heart was developed. Its ability to induce HIFU lesions on the left atrium or on the left ventricle has been demonstrated *ex vivo* (Constanciel et al. 2013a).

The aims of the present acute pilot study in the porcine model were to show the *in vivo* feasibility of inducing a cardiac thermal lesion without an intravascular device using a US-guided endoesophageal HIFU approach, to explore the accuracy of the US guidance and to evaluate the immediate safety of the procedure.

MATERIALS AND METHODS

Ultrasound equipment

Two different endoesophageal US-guided HIFU prototypes were used (Table 1, Figs. 1a and 1b). These consisted of a therapeutic 8-element transducer (Imasonic, Voray sur l'Ognon, France) operating at a frequency of 3 MHz, and included in their center was a 5-MHz 64-element commercial imaging transducer for transesophageal echocardiography (TEE) (PA5.0/64, Vermon, Tours, France). The dimensions of the probes were based on the dimensions of the human esophagus and throat anatomy (Tsao et al. 2006). The probe head housing was 18 mm in diameter and 50 mm in length. The first probe was mounted on a "rigid" tube, which was 800 mm long and 16 mm in diameter, and the second prototype was "flexible." The prototypes were driven by a multi-channel amplifier (Image Guided Therapy, Pessac, France), which can generate up to 20 W per channel. Electrical circuits using inductors were constructed for impedance matching 50 Ohms between the amplifier driving the system and each transducer element. Acoustic power measurements were first performed with the acoustic balance method

Table 1. Characteristics of the two TEE-guided HIFU endoscopes used in the present *in vivo* study

Technical characteristics	1st prototype	2nd prototype
Endoscope body		
Body type	Rigid	Flexible
Length (cm)	80	100
Diameter (mm)	16	11
Probe head housing		
Length (mm)	50	
Diameter (mm)	18	
HIFU transducer prototype		
Transducer type	Focused annular-array	
Natural focusing/Radius of curvature (mm)	40	
Aperture (mm)	30	
Truncation (mm)	14	
Total surface area (cm^2)	3	
Number of element	8	
Elements geometry and conformation	Isosurface concentric rings: 1 full and 7 truncated	
Internal diameter of the smallest ring/of the central hole for on-board TEE (mm)	12	
Working frequency (MHz)	3	
Electronic focusing range (mm)	15–55	
Maximum acoustic intensity at transducer surface (W/cm^{-2})	9	13
Commercial TEE probe (PA5.0/64; Vermon)		
Transducer type	Linear phased-array	
Number of element	64	
Element pitch (mm)	0.145	
Working frequency (MHz)	5	
Frequency bandwidth at −6 dB (%)	55	
Geometry of the acquired US image	Sectorial	
US image depth (mm)	15	
Angular aperture	90	
Frame rate (Hz)	34	

HIFU = high-intensity focused ultrasound; TEE = transesophageal echocardiography.