Intracardiac Myocardial Elastography in Canines and Humans *In Vivo*

Julien Grondin, Elaine Wan, Alok Gambhir, Hasan Garan, and Elisa E. Konofagou

***Abstract*—Intracardiac echocardiography (ICE) is a useful imaging modality which is used during RF ablation procedures to identify anatomical structures. Utilizing ICE in conjunction with myocardial elastography (ME) can provide additional information on the mechanical properties of cardiac tissue and provide information on mechanical changes caused by ablation. The objective of this study was to demonstrate that ICE can be used at high frame rate using a diverging beam transmit sequence to image myocardial strain and differentiate myocardial tissue properties before, during, and after ablation for a clinical ablation procedure. In this feasibility study, three normal canines and eight patients with atrial fibrillation (AF) were studied *in vivo*. A 5.8-MHz ICE transducer was used to image the heart with a diverging beam transmit method achieving 1200 frames per second (fps). Cumulative axial displacement estimation was performed using 1-D cross-correlation with a window size of 2.7 mm and 95% overlap. Axial cumulative strains were estimated in the left atrium (LA) and right atrium (RA) using a least-squares estimator with a kernel of 2 mm on the axial displacements. In the canine case, radial thickening was detected in the lateral wall and in the interatrial septum during LA emptying. For AF patients, the mean absolute strain in the ablated region was lower (6.7 ± 3.1%) than before the ablation (17.4 ± 9.3%) in LA at the end of the LA emptying phase. In the cavotricuspid isthmus (CTI) region, mean absolute strain magnitude at the end of the RA emptying phase was found to be higher during ablation (43.0 ± 18.1%) compared with after ablation (33.7 ± 15.8%). Myocardial strains in the LA of an AF patient were approximately 2.6 times lower in the ablated region than before ablation. This initial feasibility indicates that ME can be used as a new imaging modality in conjunction with ICE in RF ablation guidance and lesion monitoring.**

I. Introduction

A. RF Ablation of Atrial Fibrillation

Atrial fibrillation (AF) is a disorder of heart rhythm that is estimated to affect 2.3 to 5.1 million people in the United States and is expected to involve more than 5.6 to 12.1 million by 2050 [1], [2]. RF ablation can be used to treat AF. The procedure requires percutaneous insertion of catheters into the heart and application of an alternating electrical current on arrhythmogenic regions of the myocardium to generate lesions [3], such as electrical isolation of the pulmonary veins. Being able to identify and characterize lesion gaps as well as transmurality of lesions is of paramount interest to improve the success rate of ablation procedures and decrease the need for repeat ablations [4]–[6]. Determinants of lesion transmurality include contact force applied by the catheter on the myocardium [7], impedance [8], power, temperature [9], and duration of ablation [10]. However, there are currently no technologies clinically available that allow for real-time assessment of tissue changes caused by RF delivery. Ultrasound techniques such as contrast-enhanced ultrasound [11], [12] or elastography [13] have also been considered to monitor ablation lesions but has been mainly applied to kidney or liver and used externally placed ultrasound probes which cannot easily be integrated in a clinical cardiac ablation setting.

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B. Intracardiac Echocardiography During RF Ablation

Intracardiac echocardiography (ICE) is commonly used to provide real-time imaging of the heart to identify anatomic structures and guide RF ablation. Using ICE as an imaging modality for lesion characterization would forego the need for additional equipment or modification of the ablation procedure or clinical setup.

ICE has previously been used to characterize endocardial lesions based upon tissue swelling and increase in tissue echogenicity [3], [14]. However, this technique tends to overestimate the lesion size and its efficiency remains to be proven. In addition, echogenicity does not provide quantitative or qualitative information about the mechanical characteristics of the tissue and its changes during RF delivery. Although tissue temperature can indicate tissue desiccation and denaturation of tissue proteins [15], which can result in an increase in elastic modulus of tissues [16], [17], catheters currently used for RF ablation are irrigated-tip catheters, which provide catheter-tip temperature, but do not provide direct tissue temperature measurements. None of the current feedback information, such as temperature, power, impedance, and ablation duration, provides information on tissue stiffness or contractility which decreases during ablation. Previous studies have reported a decrease in atrial strain or strain-related parameters in humans [18] and canines [19] who received RF ablation six month prior.

C. Intracardiac Echocardiography for Myocardial Tissue Mechanics Assessment

So far, ICE has been used in the field of cardiac motion estimation. Wang *et al.* have assessed strains in the anterior region of the myocardium in a canine model using M-mode tissue Doppler imaging (TDI) [20]. However, this method required a compromise between the frame rate and the field of view of the heart and only a specific region of the myocardium was investigated. Another previous study assessed strain rate from M-mode tissue velocity from ICE imaging in the porcine model [21], but this study presented shortcomings similar to the previous one. Yue *et al.* have assessed myocardial strain in a canine model using speckle tracking on B-mode images [22]. This method suffered nevertheless both from the loss of phase information due to envelope detection and from a low frame rate (30 fps) which affected the quality of motion estimation. More recently, acoustic radiation force impulse (ARFI) has been applied to ICE to characterize myocardial stiffness by measuring shear wave velocity [23]. ARFI has also been used with ICE to assess RF ablation lesions in canine and porcine models [24], [25]. However, these studies used a depth of field of less than 3 cm, which required the ICE catheter to be proximal to the surface of the myocardium and did not allow for a full clinical imaging window.

Herein, we present a study in humans which, by using myocardial elastography (ME) in adjunct with ICE, allows for assessment of the mechanical properties of the myocardium, a surrogate marker of electrical conduction, and thus can be used to characterize the extension and efficacy of ablation lesions. It has recently been reported that the LA strain can predict the success of AF ablation [26]–[28]. Previous studies have shown that strains could be obtained with ME at a high frame rate and a large field of view of the heart [29]. High-frame-rate ultrasound imaging can be achieved with techniques such as composite imaging [30] or parallel beamforming using plane wave [31] or diverging beams [32], [33]. Diverging beams have the advantage of reconstructing a large field of view at a very high frame rate. To the authors' knowledge, high-frame-rate imaging using diverging beams has never been used with ICE. In this study, our objective was 1) to use diverging wave imaging and parallel beamforming with ICE to image myocardial strain at high temporal resolution during atrial emptying in canines and humans *in vivo* and 2) to demonstrate that strain imaging with ICE can differentiate myocardial tissue properties before, during, and after ablation for a clinical ablation procedure.

II. Methods

A. Canine Study

A preliminary feasibility study was performed in the canine model. Three male canines ranging from 23 to 25 kg in weight were premedicated with diazepam (0.5 to 1.0 mg/kg) injected intravenously and then anesthetized with an intravenous injection of propofol (2 to 5 mg/kg). The canines were mechanically ventilated with a rate- and volume-regulated ventilator on a mixture of oxygen and titrated 0.5% to 5.0% isoflurane. An ICE catheter was inserted into the jugular vein through a 10F introducer sheath and advanced to the right atrium (RA). The study was approved by the Institutional Animal Care and Use Committee of Columbia University.

TABLE I. Patients Scanned for Different Acquisitions.

Acquisition	Patient ID numbers
Reproducibility	#1, #2
Before and after ablation	#3, #4, #5
Before and during ablation	#3, #6
After (t) and after ($t + \Delta t$) ablation	#4, #6, #7
During and after ablation	#8

B. Clinical Study

For the clinical study, eight patients (61.1 ± 15.1 years old) underwent AF ablation, during which ICE was routinely used as a component of their procedure. The ICE catheter was inserted into the femoral vein and advanced under direct fluoroscopic guidance as per standard protocol to the right atrium. B-mode images of the right and left atrium with the ablation catheter in the field of view were recorded. Ultrasound data were acquired before and/or during and/or after ablation in similar echocardiographic views and similar heart rhythm (Table I). Two patients (Patient #1 and Patient #2) were investigated to carry out a reproducibility study. The number of patients for which data were acquired both before and after ablation was $N = 3$ (Patient #3, Patient #4, and Patient #5). The number of patients for which data were acquired both before and during ablation was $N = 2$ (Patient #3 and Patient #6). The number of patients for which data were acquired after ablation at different times was $N = 3$ (Patient #4, Patient #6, and Patient #7). The number of patients for which data were acquired both during and after ablation was $N = 1$ (Patient #8). RF ablation was either performed around the pulmonary veins, and/or cavotricuspid isthmus (CTI), and/or left atrium (LA). The study protocol was approved by an Institutional Review Board of Columbia University and informed consent was obtained before the study.

C. Ultrasound Acquisition

A 5.8-MHz ICE catheter with 64 elements and 13 mm active aperture (ViewFlex PLUS ICE catheter, St. Jude Medical, St. Paul, MN) on an ultrasound system (Viewmate Z, St. Jude Medical) was used. The imaging depth was set to 90 mm to be able to image at least one heart chamber, such as the left atrium. The ultrasound system

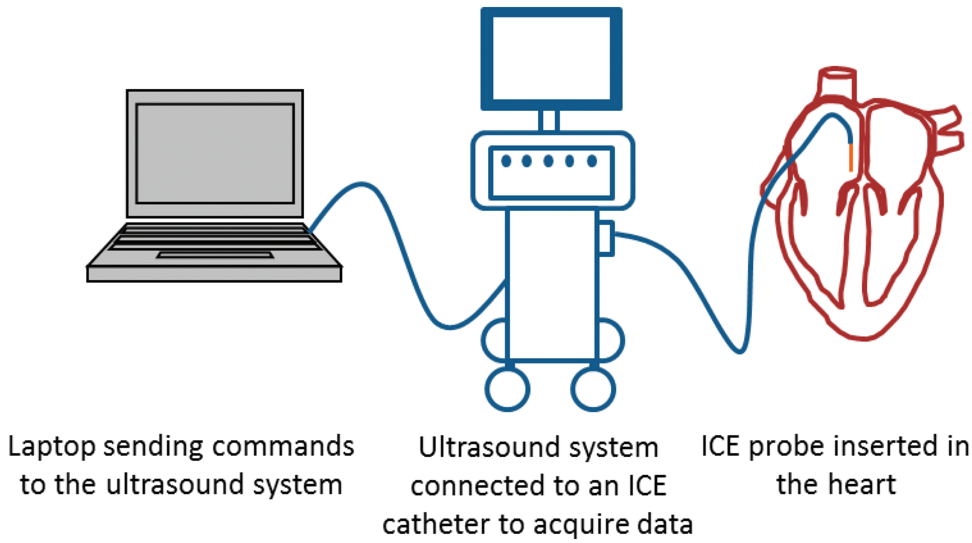

Fig. 1. Experimental setup. An ICE catheter connected to an ultrasound system is inserted into the right atrium of canines through the jugular vein or through the femoral vein in humans. A laptop is used to send commands to the ultrasound system to set the imaging parameters and to acquire and save the RF data.

was connected to a computer via a serial cable (Fig. 1), which allowed control over the parameters and the acquisition as well as data transfer to a hard drive connected to the system [34]. High-frame-rate imaging was achieved by reconstructing the entire frame from a single-beam transmit. An unfocused diverging beam transmit was used to achieve a frame rate of 1200 fps, which was the highest frame rate achievable by this scanner at a depth of 90 mm (Fig. 2). To send an unfocused beam with a diverging angle of 90°, a virtual source was placed 6.5 mm behind the transducer, which corresponds to half the size of the active aperture. The virtual source was centered relative to the transducer. The distance between the virtual source

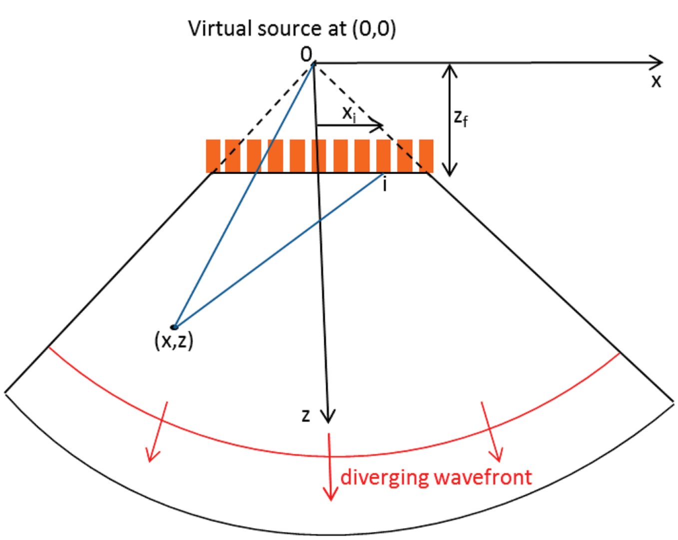

Fig. 2. Diverging beam transmit illustration. Delays between a virtual source located at a distance z_f behind the probe and all the elements of the transducer produce a diverging beam (in red). The time of flight between the emission from the transducer and the reception on the ith element located at (x_i, z_f) of the signals reflected from point of the grid located at (x, y) was computed.

and each element of the transducer was computed to obtain the time delay to apply to each element to obtain a diverging wave. The 24 central elements had no apodization, whereas the remaining 20 elements on each side had a weak apodization in transmit. Prior to *in vivo* application, the transmitted unfocused beam was characterized with a hydrophone (HGL-0200, Onda Corp., Sunnyvale, CA) in a water-filled tank. The hydrophone was set on a mechanical stage and the probe was attached to the wall of the tank. The hydrophone was moved along the lateral direction at three different axial depths (2, 50, and 90 mm) and the maximum pressure was obtained for each lateral position.

Echocardiographic views of LA were acquired for the canine study, whereas views of the LA as well as RA and right ventricle (RV) in the region of the CTI were acquired in humans.

The in-phase and quadrature (IQ) data were acquired on all the 64 channels in parallel and stored in the system buffer (Fig. 3). At 90 mm depth and 1200 fps, the buffer of the ultrasound system could store up to 620 ms of IQ signals. Conventional B-mode images were acquired at 35 fps at the same location to help for structure identification. The data were transferred to a computer for off-line processing.

D. RF Signals Reconstruction

The RF signals were obtained from the IQ data and upsampled to 50 MHz to increase the quality of the motion estimation. The RF signals were then reconstructed using a standard delay-and-sum algorithm described as follows. A grid of points onto which the RF signals would be reconstructed was defined in a polar coordinate system on a region of 90° field of view with 128 lines and depth of 90 mm with a radial grid step of 15.4 µm and for which the origin was the virtual source. The time of flight, T_f,

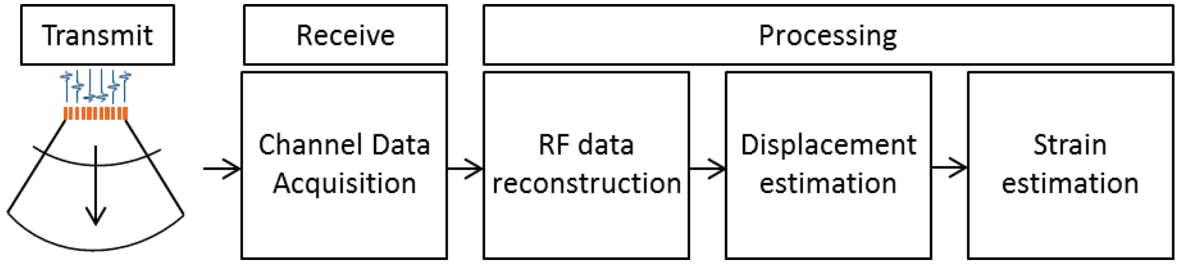

Fig. 3. Flowchart of the acquisition and processing procedure. Delays are applied to each channel of the transducer to transmit a diverging beam. The received signals are acquired on each channel. The RF data are reconstructed using a delay-and-sum method. The RF signals are cross-correlated to estimate displacements. Strains are obtained by taking the gradient of the displacement using a least-squares estimator.

between the emission from the transducer and the reception on all the elements of the signals from every point of the grid was computed as follows:

$$T_\mathrm{f} = T_\mathrm{t} + T_\mathrm{r} - T_\mathrm{d} + T_\mathrm{b}, \quad (1)$$

where

$$T_\mathrm{t} = \frac{\sqrt{x^2 + z^2}}{c} \quad (2)$$

denotes the time of flight from the virtual source to a point of the grid located at (x, z) and c is the speed of sound, assumed to be 1540 m·s^{-1}.

$$T_\mathrm{r} = \frac{\sqrt{(x - x_i)^2 + (z - z_\mathrm{f})^2}}{c} \quad (3)$$

is the time of flight from the pixel located at (x, z) to the ith element of the transducer located at (x_i, z_f).

$$T_\mathrm{d} = \frac{z_\mathrm{f}}{c} \quad (4)$$

is the time that must be removed from T_f to take into account the beginning of acquisition when emitted from the center element located at $(0, z_\mathrm{f})$, and T_b takes into account a bulk delay related to the ultrasound system and the propagation in the lens at the surface of the transducer (Fig. 2). The amplitude of each RF channel signal at each point of the grid was then computed using 1-D linear interpolation. Receive focusing at each point of the grid was performed by summing the interpolated amplitude of the RF channel signals across all the elements of the transducer. The reconstruction operation was performed on a GPU (Tesla C2075, NVIDIA Corp., Santa Clara, CA) to increase the computation speed. A B-mode image was obtained (Fig. 4) from the reconstructed RF data by a Hilbert transform and a manual segmentation was performed to retrieve the myocardium. The conventional B-mode provided landmarks to assist the myocardial segmentation. The contrast-to-noise ratio (CNR) was computed for both the reconstructed B-mode obtained from the diverging wave transmit and for the conventional B-mode for approximately the same view and same phase of the cardiac cycle. The CNR was defined as [35]

$$\mathrm{CNR} = \frac{2(\mu_\mathrm{t} - \mu_\mathrm{b})^2}{\sigma_\mathrm{t}^2 + \sigma_\mathrm{b}^2},$$

where μ_t and μ_b are the mean of the amplitude inside the region of interest corresponding to the tissue and to the background, respectively, and σ_t and σ_b are the standard deviation of the amplitude inside the region of interest corresponding to the tissue and to the background, respectively.

E. Displacement and Strain Estimation

The displacement between two successive frames was estimated by normalized 1-D cross-correlation [36] with a window length of 2.7 mm (10 wavelengths) [37] and 95% overlap. The displacements were then integrated during atrial emptying (passive and active) to obtain the cumulative displacements. The relative myocardial wall displacement was therefore used as a surrogate to determine the emptying phase. During emptying of a heart chamber, its volume decreases. Displacement images obtained at high temporal resolution allow for identifying the beginning and the end of the inward motion. For LA imaging, the phase from maximal size to minimal size of the LA includes both LA conduit (passive emptying) and contractile (active emptying) function. Although out-of-plane motion can affect the apparent size of the LA in the echocardiographic view, the LA maximum volume corresponds to the beginning of LA conduit and LA minimum volume corresponds to the end of the LA active emptying phase [38], [39]. The patients for which no clear inward motion was observed were discarded from the study. Strain at the end of the atrial emptying phase was defined as the strain accumulated from the beginning to the end of the atrial inward motion. Previous studies recommended defining end-diastole (systole) as the frame in the cardiac cycle in which the cardiac dimension is the largest (smallest) [40]. The selection of the frames corresponding to emptying was performed using similar criteria such as myocardial wall relative displacement for the ablation and the nonablation cases. For RA and RV imaging, the closure of the tricuspid valve was used as a reference for the phase selection. Cumulative axial strains were computed from cumulative axial displacements by applying a least-squares estimator [41] with a kernel equal to 2 mm using a Sav-

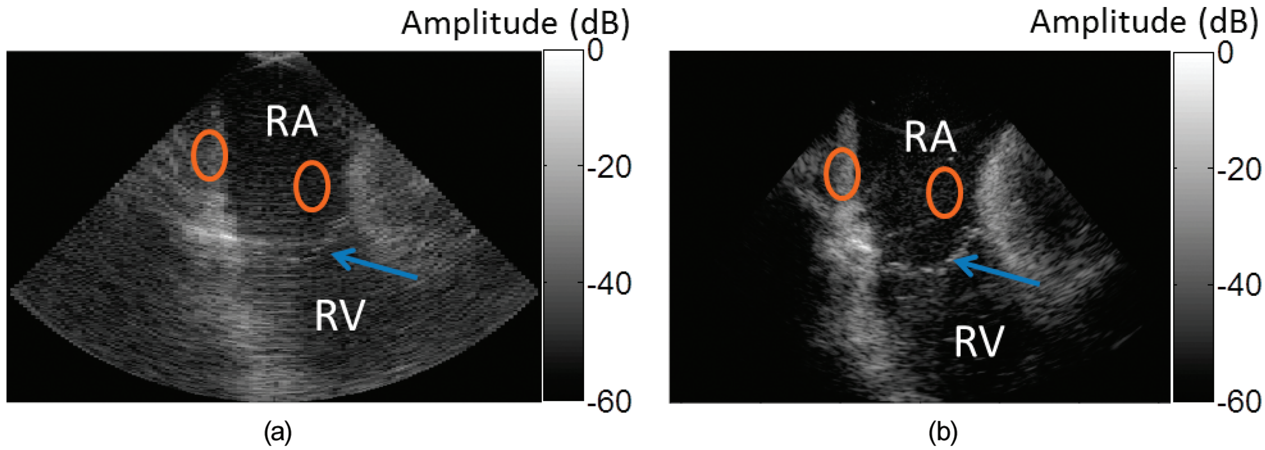

Fig. 4. B-mode for a reconstructed image (a) from a single diverging wave transmit and (b) for a conventional line-by-line acquisition. RA and RV denote the right atrium and ventricle, respectively. The blue arrow points to the tricuspid valve. The ellipses in orange indicate the regions chosen to compute the contrast-to-noise ratio. The ellipse on the RA wall was used for the tissue and the ellipse inside the RA cavity was used for the background.

itzky–Golay filter [42] to decrease the noise amplification resulting from gradient operation.

A region of interest of approximately the same size and location was selected in the lateral wall of each canine LA to compute the value of the cumulative axial strain at the end of the atrial emptying phase. To compare before, during and after ablation in patients, strains were estimated approximately at the same location and approximately the same phase of the cardiac cycle and during the same rhythm (normal sinus rhythm, AF or atrial flutter) in a region of interest of approximately 5×5 mm^2. The size of the region of interest was chosen to be slightly larger than the size of the tip of the ablation catheter because of heat diffusion as well as catheter movement during the ablation. The mean and standard deviation of the strain in the selected region of interest were computed. In the canine study or when comparing different groups (before, during, and after), the mean and standard deviation reported are computed across the different individuals in the group.

To investigate the reproducibility of our technique, B-modes and RF channel data were acquired twice with approximately one minute between each acquisition in the same echocardiographic view without moving the ICE catheter in two patients. For one patient, the LA was imaged, whereas for the other patient, the RA and RV were imaged. In all the cases, the ultrasound data were acquired before ablation and during sinus rhythm. Strains at the end of the atrial emptying phase were imaged and compared for both acquisitions in each patient.

III. Results

Myocardial displacement and strain were imaged with ICE at 1200 fps using parallel beamforming in three canines and eight humans *in vivo*. The acquisition duration was less than the duration of a cardiac cycle. For each acquisition, either the entire emptying or filling phase could be obtained, but not both. The acquisition duration was also less than the duration of the ablation at a specific location, which hindered demonstration of the evolution of the strain as a function of ablation time. The ultrasound data were acquired during normal sinus rhythm, AF, or atrial flutter. Conventional B-mode images were also acquired to assist myocardial segmentation. The CNR was computed for both the reconstructed B-mode obtained from a diverging wave imaging and for a conventional B-mode. The CNRs for the reconstructed and the conventional B-modes were 5.1 and 9.3, respectively.

A. Canine Study

Axial displacement and strain were assessed in the LA from ICE acquisitions in LA short-axis view of three canines during atrial emptying (Fig. 5). The ICE probe is located in the RA and oriented toward the LA. Axial displacements are shown at the end of the LA emptying phase in Figs. 5(a)–5(c). Displacements in the lateral (anatomical) direction are in blue whereas displacements in the medial direction are in red. The interatrial septum wall is detected moving in the lateral direction (blue) whereas the left lateral wall is moving in the medial direction (red). A schematic diagram indicating the LA wall displacements is shown in Fig. 5(g). The corresponding strains [Figs. 5(d)–5(f)] show that positive strain in red (radial thickening) is observed in the lateral wall and the interatrial septum, whereas negative strain in blue (circumferential shortening) occurs in the anterior and posterior walls. Similar displacement and strain patterns are observed for the three canines. The mean absolute axial cumulative strain at the atrial emptying phase in the selected region of interest in the lateral wall across the three dogs was $15.8 \pm 12.1\%$, where 12.1% reflects the variability across the three dogs.

B. Clinical Study

The reproducibility of our technique was investigated in two patients before ablation in sinus rhythm. Strains at

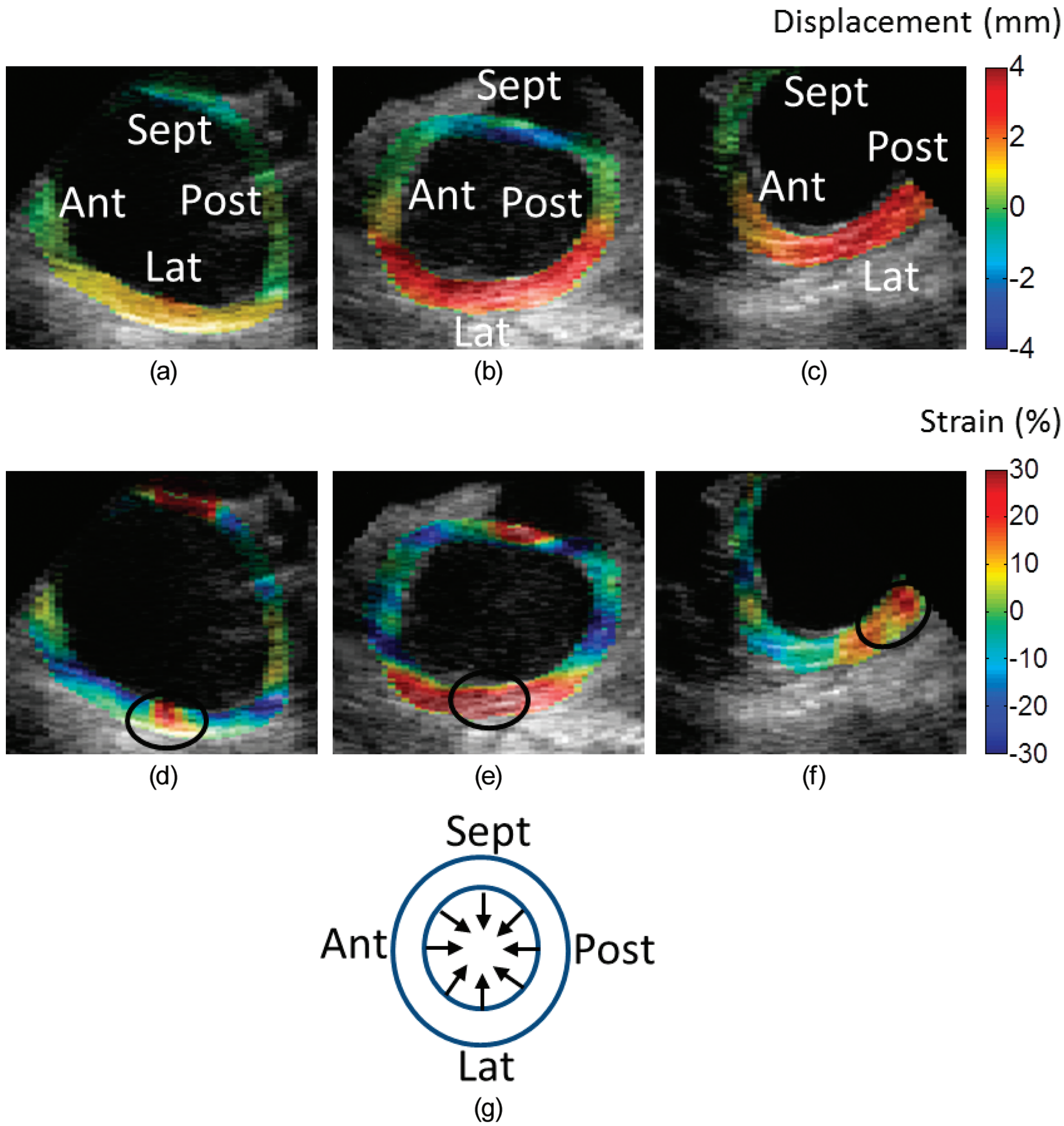

Fig. 5. [(a)–(c)] Cumulative axial displacement and [(d)–(f)] cumulative axial strain in three canine left atrium (LA) at the end of the LA emptying phase. Positive (red) displacements are in the medial direction and negative (blue) displacements in the lateral direction. The interatrial septum (Sept) wall is moving in the lateral direction whereas the left lateral (Lat) wall is moving in the medial direction. (g) A schematic diagram of the LA displacement is shown. In this view, contraction corresponds to radial thickening and circumferential shortening. Radial thickening is observed in the lateral wall and the interatrial septum whereas circumferential shortening occurs in the anterior (Ant) and posterior (Post) wall. The black ellipse indicates the region of interest for which strain was computed for comparison. Similar displacement and strain patterns are observed for the three dogs.

the end of the atrial emptying phase for two consecutive acquisitions in two different patients are shown in Fig. 6. Strain at the end of the LA emptying phase is shown for two consecutive acquisitions in Patient #1 [Figs. 6(a) and 5(b)]. Strain at the end of the RA emptying phase is shown for two consecutive acquisitions in Patient #2 [Figs. 6(d) and 5(e)]. A similar strain pattern is obtained for both acquisitions in each patient.

Displacements and strains were also estimated in the LA of AF patients before, during, and after an RF ablation procedure. Cumulative axial displacement before ablation at the end of the LA emptying phase for Patient #4 during atrial fibrillation is shown in Fig. 7(a). The ICE probe is located in the RA and oriented toward the LA. During LA emptying, the LA contracted inward [Fig. 7(e)]. The corresponding strains at the end of the LA emptying phase are shown in Fig. 7(b). In this view, radial thickening is observed in the anterior wall and absolute strain magnitude at the end of the LA emptying phase reached approximately 16.4 ± 10.1%. Axial displacements during ablation in the LA of the same patient and for approximately the same cardiac phase and rhythm are shown in Fig. 7(c). LA contracted inward. The corresponding strains are shown in Fig. 7(d). The black ellipse indicates the region of ablation and the red arrow points to the ablation catheter. The absolute strain magnitude is lower, approximately 0.9 ± 3.0%, in the region where ablation occurred, which is less than before ablation. The decrease in strain was observed in the region of ablation, whereas the regions where no ablation was performed did

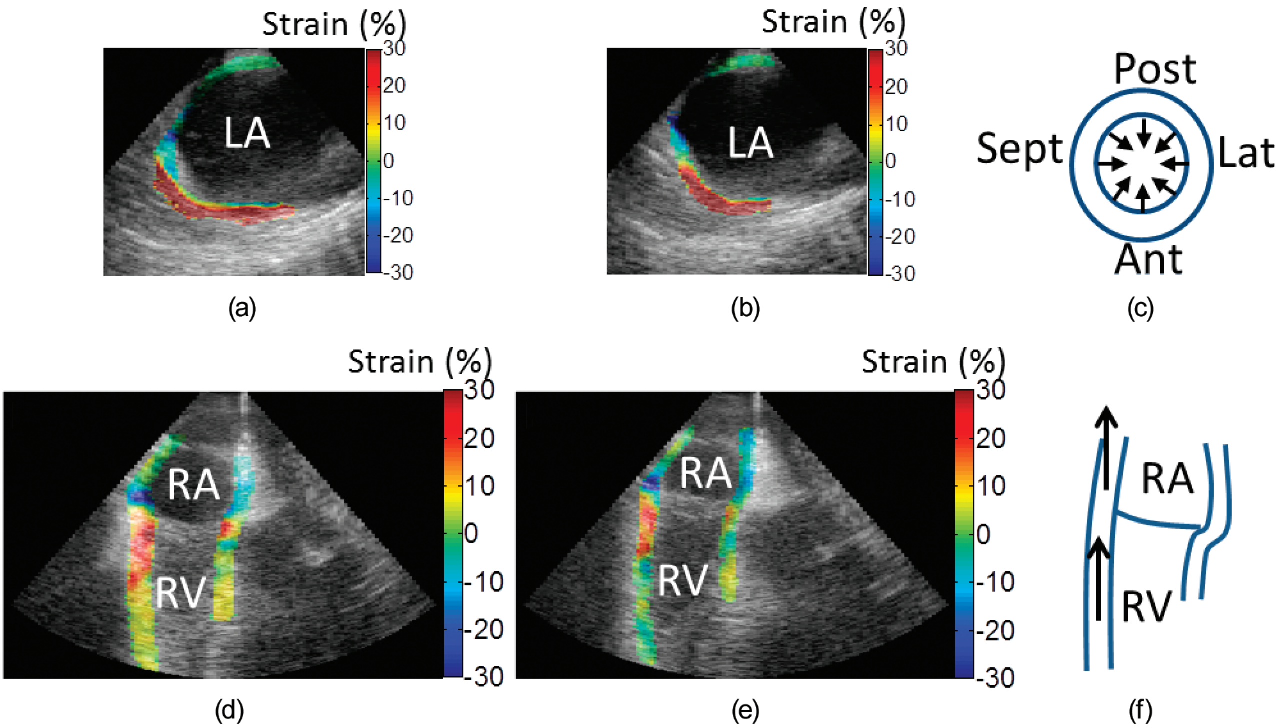

Fig. 6. Cumulative axial strain at the end of the LA emptying phase for two consecutive acquisitions in [(a) and (b)] left atrium (LA) of patient #1 and [(d) and (e)] right atrium (RA) and right ventricle (RV) of patient #2. Both patients were in sinus rhythm during both acquisitions. A schematic diagram of (c) the LA displacement for patient #1 and of (f) RA and RV displacement for patient #2 are shown. A similar strain pattern is obtained for both acquisitions in each patient.

not exhibit a significant change in strain. This decrease in strain indicates that the contractility of the myocardium is reduced in the ablated region, which indicates lesion formation.

Cumulative axial displacements and strains at the end of the RA emptying phase were also evaluated in the CTI region of Patient #6 in sinus rhythm during and after RF ablation in this region (Fig. 8). The ICE probe is located in the RA and oriented toward the right ventricle (RV). Axial displacements in the patient RA and RV during ablation are shown in Fig. 8(a). The RA and RV lateral walls moved in the superior direction [Fig. 8(e)]. The corresponding strains are shown in Fig. 8(b). In this view, RA longitudinal shortening and RV longitudinal lengthening are shown in their respective lateral walls. The absolute strain magnitude in the RA lateral wall was approximately 43.0 ± 18.1%. Axial displacements in the same patient RA and RV in the CTI region after ablation and during approximately the same cardiac phase are shown in Fig. 8(c). The RA and RV lateral walls moved in the superior direction. The corresponding strain is shown in Fig. 8(d) and was approximately 33.7 ± 15.8% in the region of ablation, which is less than before ablation. Moreover, the strain magnitude in the ablated region was decreased on the endocardial side of the myocardium more than on the epicardial side, which suggests that the transmurality of the lesion can be imaged with this method.

The strain variation at the different stages of the ablation for all patients is shown in Fig. 9. Error bars represent standard deviation in the selected region of interest corresponding to the region of ablation. Strains were compared before and after ablation for three patients totaling four ultrasound views; two ultrasound views were obtained for one of the three patients. The average absolute strain magnitude before ablation was 17.4 ± 9.3% and decreased to 6.7 ± 3.1% after ablation. Strains were also compared before and during ablation for two patients with one ultrasound view per patient. The average absolute strain magnitude was 11.3 ± 7.2% before ablation and 4.0 ± 4.4% during ablation. Strain after ablation at a certain time (ε^t) was also compared with strain after ablation later on ($\varepsilon^{t+\Delta t}$). The average absolute strain magnitude was 16.2 ± 17.7% after ablation at time t and 10.9 ± 10.7% after ablation at time $t + \Delta t$.

IV. Discussion

Characterization of thermal lesions generated by RF ablation of the heart is of paramount interest to enable real-time assessment of lesions, allowing for characterization of transmurality and gaps, which in turn may aid in long-term success of ablation procedure. Myocardial elastography (ME) is an ultrasound technique that, combined with intracardiac echocardiography (ICE), can provide information on the mechanical properties of tissues. The aim of this study was two-fold: 1) use diverging wave imaging and parallel beamforming with ICE to image myocardial strain at high temporal resolution during atrial emptying in canines and humans *in vivo*; and 2) investigating

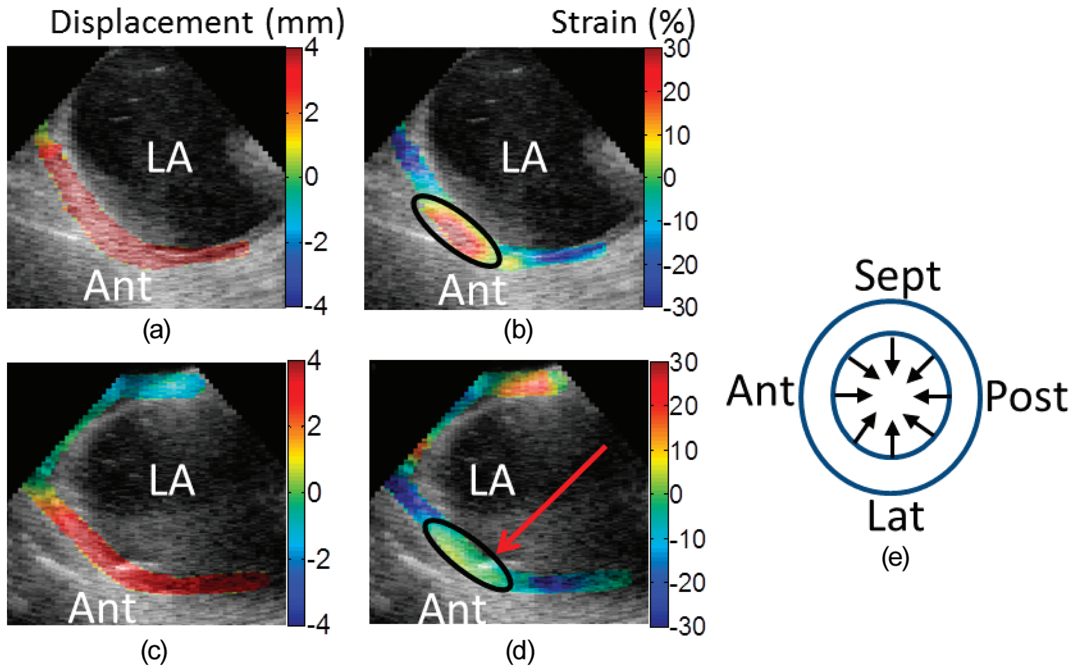

Fig. 7. [(a) and (c)] Cumulative axial displacement and [(b) and (d)] cumulative axial strain in left atrium (LA) of an AF patient at the end of the LA emptying phase. (e) A schematic diagram of the LA displacement is shown. (a) and (b) are before RF ablation, whereas (c) and (d) are during. The black ellipse indicates the region of ablation and the red arrow points to the ablation catheter. The anterior (Ant) wall moved inward. Radial thickening is observed in the anterior wall and the absolute strain magnitude is approximately 15.2 ± 9.0% before ablation and decreased to approximately 2.6 ± 3.1% in the ablated region.

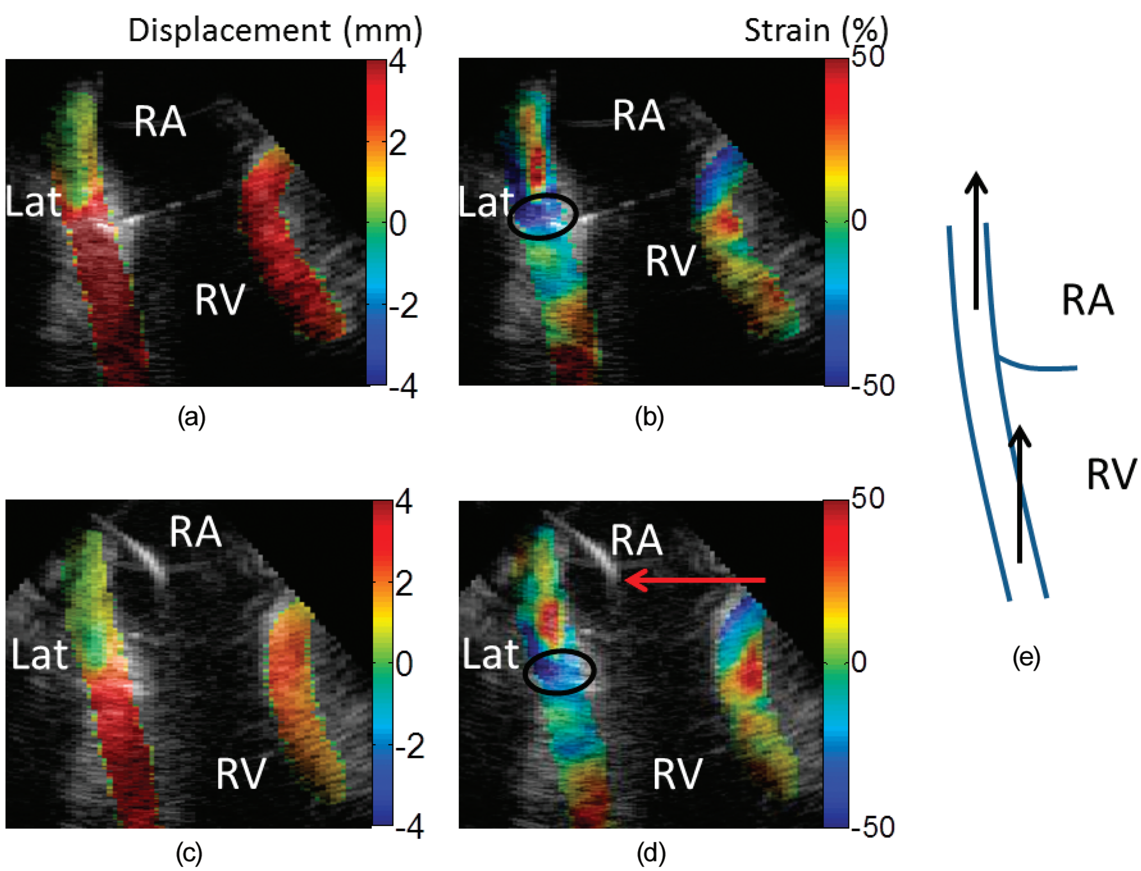

Fig. 8. [(a) and (c)] Cumulative axial displacement and [(b) and (d)] cumulative axial strain in the right atrium (RA) and right ventricle (RV) of an AF patient at the end of the RA emptying phase. A schematic of the RA and RV displacement is shown (e). (a) and (b) are during RF ablation, whereas (c) and (d) are after. The black ellipse indicates the region of ablation and the red arrow points to the ablation catheter. The lateral (Lat) wall moved toward the superior direction. In this view, positive (negative) strain corresponds to longitudinal lengthening (shortening). Longitudinal shortening is observed in the RA lateral wall whereas longitudinal lengthening can be seen in the RV lateral wall. The absolute strain magnitude in RA lateral wall was approximately 44.8 ± 15.9% during ablation and 35.1 ± 14.5% after ablation.

the difference in myocardial strains with ICE before, during, and after RF ablation during a clinical ablation procedure. The performance of diverging wave imaging was compared with that of conventional B-mode imaging by comparing the contrast-to-noise ratio (CNR) for both cases. The CNR was found to be 5.1 for the reconstructed B-mode and 9.3 for the conventional B-mode. A better contrast is obtained for the conventional B-mode because of focused transmit for each line, which gives a better lateral resolution. However, the acquisition of RF channel data for diverging wave imaging allows for a better temporal resolution compared with conventional B-mode imaging, and several studies have shown that RF signals provide significant performance advantages over envelope signals [43]–[45]. A preliminary feasibility study was conducted on three normal canines to show the feasibility of imaging axial strain with ICE at high frame rate using diverging waves and to assess the performance of the ME method with ICE. Eight patients undergoing RF ablation which required use of ICE during ablation delivery in their left atrium and cavotricuspid isthmus (CTI) were then investigated to show the initial feasibility of clinical application of the technique. This method can be of significant interest for the assessment of lesion location induced by RF ablation during the ablation procedure to ensure the efficiency of electrical isolation and conduction block to treat the arrhythmia because mechanical contraction at a region of the myocardium follows electrical activation of the same region [46].

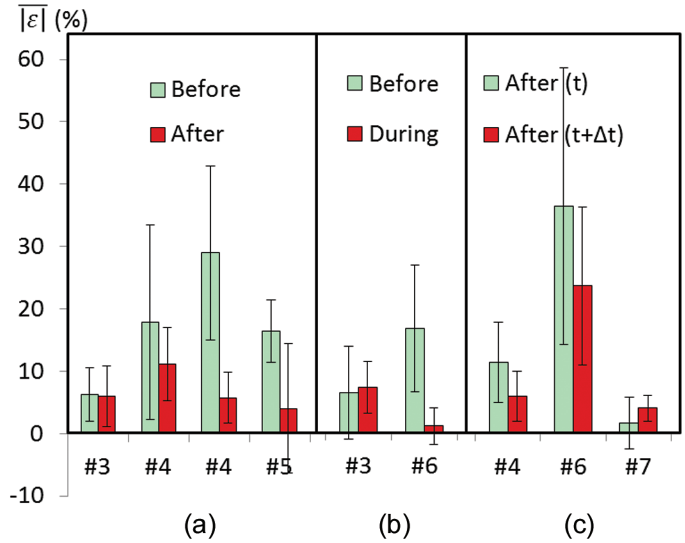

Fig. 9. Average absolute value of strain ($\overline{|\sigma|}$) at the end of the atrial emptying phase in the region of ablation for different patients (#). Error bars represent standard deviation in the selected region of interest corresponding to the region of ablation. (a) Strain before and after ablation are compared for three patients totaling four different views. (b) Strain before and during ablation are compared for two patients totaling two different views. (c) Strain after ablation at a certain time (t) and later on a time ($t + \Delta t$) are compared for three patients totaling three different views.

A. Canine Study

In the canine study, ME was performed in the LA of three normal canines (Fig. 3). Axial displacements and strains were accumulated during LA emptying. The orientation of the ICE transducer relative to the LA chamber allowed estimation mainly in the radial (in septum and lateral regions) and circumferential (in anterior and posterior regions) directions. Strains at the end of the LA emptying phase indicated radial thickening (red) in the lateral wall and the interatrial septum, whereas circumferential shortening (blue) occurred in anterior and posterior region. This was consistent with the LA displacement, which showed that the interatrial septum wall moved in the lateral direction (blue) whereas the left lateral wall moved in the medial direction (red). Similar axial strain patterns were found in the three dogs. These preliminary findings point to the potential of ME to be combined with ICE to pinpoint successful delivery of ablation lesions as demarcated by changes in tissue mechanics after ablation.

B. Clinical Study

The reproducibility of our technique was investigated in two patients before ablation in sinus rhythm. Similar strains at the end of the atrial emptying phase were obtained for two consecutive acquisitions in each patient, which indicates a good reproducibility of axial strain imaging using diverging wave imaging with ICE. Feasibility was tested afterward in a clinical study, in which AF patients underwent ICE before, during, and after RF ablation. Axial displacements and strains were obtained during LA or RA emptying. The average absolute value of strain at the end of the atrial emptying phase was found to be lower after ablation (6.7 ± 3.1%) than before (17.4 ± 9.3%) in approximately the same region. The average value of strain after ablation was 2.6 times lower than before ablation. This decrease in strain was concluded to be due to local stiffening of the tissue caused by the thermal ablation. Also for another set of ultrasound views, the average absolute value of strain at the end of the atrial emptying phase was found to be lower during ablation (4.0 ± 4.4%) than before (11.3 ± 7.2%) in approximately the same region. The average value of strain during ablation was 2.8 times lower than before ablation. For another set of ultrasound views, strain after ablation at a certain time was also compared with strain after ablation later on, following several ablations in between. The average absolute strain magnitude was 16.2 ± 17.7% after ablation and 10.9 ± 10.7% 5 to 20 min after ablation. The average value of strain after ablation at time $t + \Delta t$ was 1.5 times lower than after ablation at time t.

Similarly, cumulative axial displacements and strains were obtained in the RA and RV regions during RA emptying during and after CTI ablation (Fig. 8). In this view, only longitudinal displacements and strains in the lateral wall could be estimated. At the end of the atrial emptying phase, the RA and RV lateral walls moved in the superior direction. At the end of the atrial emptying phase, absolute strain was 43.0 ± 18.1% during ablation and 33.7 ± 15.8% after ablation.

In this study, for the first time to the authors' knowledge, the feasibility of myocardial strain estimation using RF signals at high temporal resolution and high line density with ICE during a clinical ablation procedure was shown. High temporal resolution entails good motion estimation, and thus good strain quality, because it is less subject to decorrelation [47], [48]. Atrial strain imaging can be used to characterize the mechanical properties of the atria transmurally as well as along the myocardium. This is of key interest to assess the efficacy of lesions to inhibit conduction, because conduction recovery was shown to be related to the non-transmurality and gap between lesions generated during ablation. In particular, the RF ablation procedure of AF, although usually initiated with pulmonary vein isolation, can also include targeted sites for linear ablation such as the LA roof, the anterior and posterior walls, or CTI in the RA [3]. Thus, being able to characterize thermal lesions in these regions would improve the assessment of efficacy of lesion delivery. In this study, we have shown that strain can be estimated in the LA and RA during ablation. This study also shows that this technique can be applied to image the heart under different cardiac rhythms, because images were taken in normal sinus rhythm, AF, and atrial flutter. We observed a decrease in strain during and after ablation in the LA and the RA, which indicates a change in tissue mechanics. Several studies have investigated the effect of ablation on LA contractility. Boyd *et al.* reported that LA strain during atrial relaxation and strain rate during atrial contraction were lower in patients who underwent RF ablation of AF and maintained sinus rhythm at 6-month follow-ups than normal controls [18]. The global left atrial strain in patients who underwent RF ablation was 2.4 times lower than in normal controls. Although not expressing the same quantity as the ratio calculated in this study, this ratio reflects a change of mechanical properties resulting from ablation, and was found to be in the same order of magnitude as that found in this study. They attributed this observation to atrial scarring and loss of atrial myocardial mass. Schneider *et al.* observed, on the other hand, that patients who remained in sinus rhythm three months after RF ablation of AF had increased strain in LA during emptying and diastole, whereas patients who had recurrent AF after three months tended to have decreased strain in LA compared with before ablation [49]. However, in these previous studies, atrial function in ablated patients was measured after several months of follow-up, whereas in this study, strains are measured several minutes to hours before, during, and after ablation. Eyerly *et al.* investigated the change in acoustic-radiation-force-induced displacement of myocardial tissue with ICE in canines during RF ablation [24], [50]. They reported that displacements in ablated sites were inferior to displacement in unablated sites. The ARFI-induced displacements in ablated sites were 1.9 times lower than in unablated sites. They attributed this change to lesion formation, observed in tissue pathology, caused by RF ablation. This is consistent with our results showing a decrease of strain in the RF ablated region. These results suggest that ME, when fully integrated with ICE, can be used to guide the ablation by ascertaining myocardium mechanics as a surrogate for adequate ablation delivery.

C. Limitations

The study has several limitations that can be overcome in the future. As mentioned previously, the identification of the emptying phase was obtained from the myocardial walls relative displacements and not from the ECG signal. Despite high temporal resolution of displacement images and because of manual selection, the phase of the cardiac cycle may not be perfectly matched for the different cases before, during, and after ablation in a moving heart. The inward motion was not as clear during AF as during sinus rhythm, thus indicating that AF can induce additional errors in the selection of the cardiac phase. The cardiac phase identification would be more accurate and consistent with ECG than with assessment of wall displacement. Because the phase selection was performed from the beginning to the end of the LA inward motion, the relative contribution of LA conduit and contractile function to strain at the end of the atrial emptying phase and to the change in strain was not assessed. The synchronous acquisition and storage of the ECG with RF data was not implemented for the purposes of this study but is ongoing.

The selection of the same region of interest before, during, and after ablation on the diverging wave images and on the B-mode images was performed manually by visually identifying landmarks such as the position of heart valve. Despite the efforts made to obtain similar ultrasound views before, during, and after ablation on the diverging wave images and on the B-mode images, there could be a mismatch on the selected region of interest. This could explain why the strain is slightly higher during ablation than before ablation for patient #3. Because only the axial component is estimated, this technique is angle-dependent [51], [52]. However, the comparison in strain was performed before, during, and after ablation on the selected ROIs. The average value of strain after ablation was 2.6 times lower than before ablation. This change in strain is mainly due to the ablation than to the error because of the imperfectly matched ROIs. If different ROIs are compared, different strain values will be obtained both due to a strain inhomogeneity inherent to the mechanical properties of the tissue and to the angle dependency. The strain value can therefore be under- or overestimated based on the inherent strain distribution in the tissue and on insonification angle relative to the orientation of the myocardial wall. Also, radial thickening and circumferential and longitudinal shortening occur during atrial systole. Therefore, if the axial direction is mainly aligned with the radial direction, positive strain will be obtained, whereas negative strain will be obtained if the axial direction is mainly aligned with the circumferential or longitu-

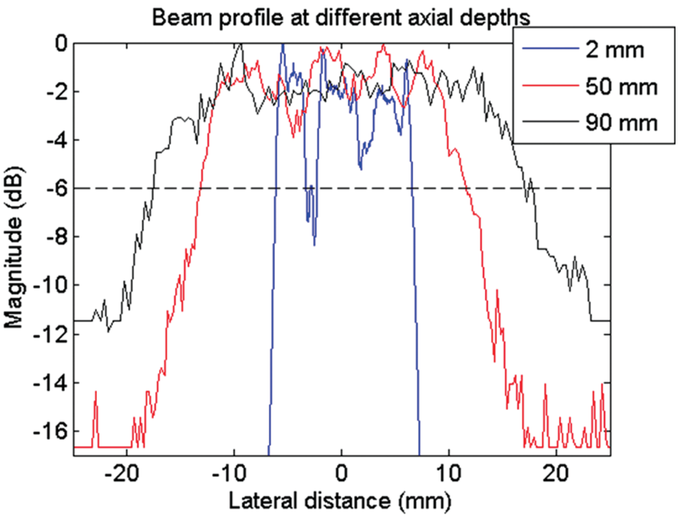

Fig. 10. Beam profile of the ICE catheter during diverging beam transmit at 2 mm (blue), 50 mm (red), and 90 mm (black) axial depths. The dashed line is the magnitude −6 dB.

dinal direction. It has to be noted that angle independence can be achieved by estimating the lateral displacement and strain and therefore deriving the angle-independent radial and circumferential strain [29]. However, that goes beyond the scope of this study.

In this study, high frame rate was obtained with parallel beamforming using a diverging wave transmit sequence. One frame was obtained from a single firing and yielded a poor lateral resolution. Spatial compounding of diverging waves can be used to increase the lateral resolution, but at the cost of decreasing the frame rate, which would entail more decorrelation. The trade-off between compounding and frame rate to obtain the best elastographic signal-to-noise ratio is currently under investigation.

The pressure profile was measured in the lateral direction at 90 mm axial depth indicates a beamwidth of approximately 35 mm at −6 dB (Fig. 10). The transmit sequence was currently not fully optimized and yielded a transmit beam with a relatively weak divergence because of apodization on the lateral elements of the transducer. Modifications of the transmit sequence are currently being performed. These improvements should entail more accurate motion estimation on the outer regions.

Finally, this study was performed in three canines without RF ablation and eight humans *in vivo* during a clinical RF ablation procedure. The results presented here demonstrate the clinical feasibility of incorporating this imaging modality into everyday practice. Further studies will be needed to include a higher number of patients to further assess the performance of the method and also to assess the applicability of this imaging technique in other chambers of the heart such as the right and left ventricle during VT ablation. An ablation study on canines must also be performed to investigate the relationship between mechanical properties of the myocardium in ablated regions and lesion features that can be obtained with histology.

V. Conclusions

This preliminary feasibility study demonstrated that myocardial strains can be imaged with ICE at high temporal resolution and high line density in canines and humans *in vivo*. The ablated regions in the human myocardium were shown to have lower strains than before ablation. Some improvements are currently being developed to obtain a more accurate myocardial strain characterization. Myocardial elastography applied intracardially can be used to visualize thermal lesions during RF ablation.

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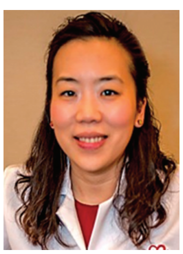

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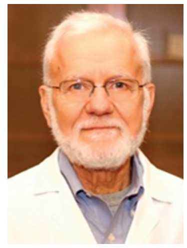

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