Visualization in Propagation of Electric Excitation in Human Heart
(心筋壁上の電気的興奮の心筋応答の超音波による可視化)

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Abstract

Conventional echocardiography visualizes cross-sectional images, motion, and torsional deformation during contraction of the heart. However, it is restricted to static configurations or large and slow motion. We have previously found that minute pulsive vibration occurs just after electrical stimulation of the extracted papillary muscle of a rat [Acoust Sci & Tech 2003;**24**:17]. By applying a novel ultrasound-based method [IEEE UFFC 1997;**44**:752] to human hearts, we were able to successfully measure the spontaneous response of the myocardium to electrical excitation [UMB 2009;**35**:936]. In the present study, we visualize the propagation of the myocardial response of the electric excitation in human hearts during systole. In the parasternal short-axis view of the left ventricle (LV), the RF reflective wave along each ultrasonic beam was acquired. The number of directions of the ultrasonic transmission was restricted to 16 to maintain a high frame rate (500 Hz), and then at all of about 25,000 points set in the heart wall, the velocity components toward the ultrasonic probe were simultaneously obtained as waveforms, and their instantaneous phases of 40-Hz components were color-coded (red: come close to). The instantaneous distribution of the phase was rearranged along the circumferential direction and set in an array consecutively at every 2 ms from the time of P-wave of the ECG, precisely revealing the propagation of the velocity components in the LV circumferential direction. This novel method was applied to healthy subjects. A velocity component corresponding to the contraction was generated at the septum at a time of R-wave of ECG, and propagated slowly (0.4 m/s) in clockwise direction along the LV circumferential direction. On the other hand, just from each radiation time of the first and second heart sounds, mechanical shear was generated at the septum and propagated in counterclockwise direction. These phenomena were observed for other subjects. The propagation of the contraction will correspond to one of the layers consisting of the LV. The subtle dynamic response of the myocardium to the arrival of the electrical stimulation accurately measured in the present study will show a potential for noninvasive assessment of myocardial damage due to heart failure.

1. Introduction

Since polarization of cells does not occur in an infarcted myocardium resulting from coronary artery occlusion, electrocardiography, by which electrical potentials generated by cell polarization are measured, is an invaluable clinical tool for the diagnosis of a broad range of cardiac conditions. However, the regional properties of the myocardium cannot be obtained by electrocardiography. A combination of electrocardiographic measurement using many electrodes on the chest surface and heart-torso geometry obtained by CT has realized imaging of the spatial distribution of action potentials [1]. However, this approach is restricted to the surface of the heart. Clinical imaging tools (CT, tissue tagging MRI [2], and conventional echocardiography [3, 4]) enable visualization of cross-sectional images, motion, and torsional deformation during contraction. However, they are restricted to static configurations or large and slow motion, and measurement of minute velocity waveforms occurring just after electrical excitation in the myocardium has not been realized.

We have previously found that pulsive vibration occurs just after electrical stimulation of the extracted papillary muscle of a rat [5]. When the displacement or deformation, corresponding to the accumulation of velocity, is measured, the proximate response to the stimulation cannot be ascertained since its amplitude is too minute (about 30 μm in displacement and 0.5 mm/s in velocity). However, by applying a novel ultrasound-based noninvasive method [6, 7] to human hearts, we were able to successfully measure the proximate response of the myocardium to electrical excitation [8]. However, such measurement was limited to the two-dimensional (2D) plane corresponding to scanning of the ultrasonic beams. In the present study, the propagation of the proximate response to the electrical excitation just before the time of the R-wave (TR) of the electrocardiogram (ECG) was visualized in three-dimensional (3D) space for the first time in healthy subjects.

2. Method

By controlling a stepping motor with reference to the ECG, the ultrasound probe on the chest wall was rotated intermittingly by 7.2 degrees in each relaxation period during several successive heartbeats, and the RF reflective wave in response to each ultrasound transmission was acquired on each of several 2D planes obtained by slicing the left ventricle (LV). The number of directions of transmission in each plane was restricted to 16 to maintain a high frame rate (500 Hz) in the modified conventional ultrasound equipment (ProSound II SSD-6500, Aloka, Tokyo, Japan) and thus minute velocity could be measured as waveforms [7] (in conventional echocardiography, the frame rate is at most 60 Hz.) At all of about 10,000 points in the heart wall, the velocity waveforms toward the ultrasonic probe (origin O) on each

fan-shaped ultrasound-scanning plane were simultaneously obtained, and their instantaneous phases of 27- or 40-Hz components were color-coded. By adjusting the times $\{T_R\}$ in the several heartbeats, the instantaneous 3D distribution of the phase was reconstructed at every 2 ms, precisely revealing the propagation of the velocity waves in the LV. The results were shown for the interior wall of the front hemisphere of the LV seen from the upper back of the heart. This novel method was applied to two healthy subjects (A: 21-year-old male, B: 24-year-old male). The study was approved by the review committee of the Graduate School of Engineering, Tohoku University and the healthy subjects gave informed consent with the principles outlined in the Declaration of Helsinki. The author had full access to the data and takes responsibility for its integrity.

The achieved lower limit in the velocity measurement has been validated as being about 0.1 mm/s, which corresponds to 0.13 μm in displacement. The wavelength is about 410 μm for a typical frequency (3.75 MHz). Thus, the measurable displacement on the order of 0.13 μm corresponds to about 1/3,000 of the wavelength [8]. Such a minute vibration superimposed on the large motion cannot be noninvasively measured by any other method. The accuracy in the adjustment of the times $\{T_R\}$ was 0.2 ms, which is sufficiently smaller than the reconstructed interval (2 ms) of the 3D phase distributions.

3. Results

For subject A, Fig. 1 shows the results (1)-(35) obtained consecutively at every 5.5 ms (= 1.9 ms × 3 frames) from 80 ms prior to the time of the Q-wave (T_Q) of the ECG. Figures 1(14) and 1(24) correspond to T_Q and T_R, respectively. Figure 1 involves the following five discriminative states: (a) The velocity of the red component (0 degrees in phase toward the probe) occurred near the base side of the LV anterior wall (Fig. 1(1)) and progressed to the entire interventricular septum (IVS) (Figs. 1(2)-(10)) at a propagation speed of 0.8 m/s. (b) A wave with a yellow-green component (120 degrees in phase) was generated at the LV posterior wall and propagated counterclockwise to the IVS at a speed of 1.5 m/s (Figs. 1(11)-(20)). (c) Just after this propagation, the red component became dominant again in the entire LV wall (Figs. 1(21)-(27)). (d) Another yellow-green component occurred near the base side and propagated downward to the apical side at a speed of 1.6 m/s (Figs. 1(28)-(33)). (e) The red component became dominant again in the whole LV (Figs. 1(34)-(35)). This final time was close to the S-wave of the ECG and then the substantial contraction started.

For another healthy subject B, Fig. 2 shows the results obtained consecutively at every 7.0 ms (= 2.3 ms × 3 frames) from 42 ms prior to T_Q. The results were shown for the interior wall of the LV free wall and the right ventricular side of the IVS seen from the upper right of the

heart. Figures 2(7) and 2(15) correspond to T_Q and T_R, respectively. The change in LV states was different from those for subject A. For subject B, (a) the red component was generated at the apical side of the anterior wall, which was close to the root of the musculus papillaris posterior (Fig. 2(1)), and propagated counterclockwise to the whole LV at a speed of 0.7 m/s (Figs. 2(2)-(16)). (b) From the radiation time of the first heart sound (Fig. 2(17)), a yellow-green component was generated at the apical side of the IVS and propagated upward to the base side along the IVS at a speed of 0.6 m/s (Figs. 2(18)-(33)). (c) Finally, the red component became dominant again in the whole LV except at the root of the papillary muscle (Figs. 2(34)-(35)).

In the parasternal short-axis view of the left ventricle (LV), the RF reflective wave along each ultrasonic beam was acquired. The number of directions of the ultrasonic transmission was restricted to 16 to maintain a high frame rate (500 Hz), and then at all of about 25,000 points set in the heart wall, the velocity components toward the ultrasonic probe were simultaneously obtained as waveforms, and their instantaneous phases of 40-Hz components were color-coded (red: come close to). The instantaneous distribution of the phase was rearranged along the circumferential direction and set in an array consecutively at every 2 ms from the time of P-wave of the ECG, precisely revealing the propagation of the velocity components in the LV circumferential direction.

The result obtained by applying this novel method to healthy subject A is shown in Fig. 3. A velocity component corresponding to the contraction was generated at the septum at a time of R-wave of ECG, and propagated slowly (0.4 m/s) in clockwise direction along the LV circumferential direction. On the other hand, just from each radiation time of the first and second heart sounds, mechanical shear was generated at the septum and propagated in counterclockwise direction. These phenomena were observed for other subjects. The propagation of the contraction will correspond to one of the layers consisting of the LV.

4. Discussion

For MRI, the temporal resolution is inevitably limited by the relaxation time (14-25 ms) of the tissue in response to the magnetic excitation [9], and the in-plane spatial resolution is 1.25×3 mm. The tissue Doppler imaging technique is restricted to static configurations or large motion (> 1 mm) with low frequency components (< 30 Hz) because the detectable amplitude is greater than the wavelength (400 μm) and the temporal resolution is at most 16 ms. Therefore, it has been considered that there are no minute velocity components in the human heart walls, and none of conventional clinical imaging methodologies can detect *minute velocity waveforms* nor visualize myocardial *dynamic properties* with high temporal resolution of a few milliseconds [7].

The dynamic phenomena observed in Figs. 1 and 2 occurred in the short period around T_R. The results along the line passing through the IVS from the apical side to the base side in the 3D spaces of Figs. 1 and 2 roughly corresponds to the 1D results obtained for the apical views in Figs. 4, 6, and 7 of a previously reported study[7], since the states in all figures commonly changed from light blue, to dark blue, to red, to yellow, to green, and finally to red during the period around T_R. Thus, as described in the previous report [8], the red component generated just before T_Q would be the initial myocardial response to electrical excitation. The yellow-green components would be the propagation of the mechanical vibrations corresponding to the first heart sound, and they appear to prevent myocardial contraction during the first heart sound. (Similar results are shown in Fig. 11 of report by Yoshiara *et al.* [10] and Fig. 5 of the report by Tanaka *et al.* [11]) Finally, the red components dominant in the entire LV at the end of the first heart sound show the beginning of substantial contraction. At a few hundred milliseconds after this time, the wall thickness and the torsional deformation due to the contraction have their maxima, which are measured in the conventional method [4]. Thus, the time scale of the results obtained by the present study is completely different from that obtained by the conventional methodologies.

Physiologically, the depolarized action potentials, cyclically generated at the sino-atrial node, propagate to the Purkinje fibers, which form interweaving networks on the endocardial surface of both ventricles and transmit the impulse almost simultaneously to the ventricular endocardia at a speed of 2-4 m/s [12]. Around T_Q, based on cell-to-cell connections, the action potential starts to propagate with a speed of 0.3-1 m/s [12] to the entire wall from the Purkinje fiber-myocyte junctions on the IVS surface, where the Purkinje fibers are in contact with the myocardium. Since simple bifurcation of the Purkinje fibers into the anterior and posterior fascicles is uncommon among subjects[12], the differences such as those between the results in Figs. 1(1) and 2(1) regarding the starting points of the propagation of the red component around T_Q can be expected.

The subtle dynamic response of the myocardium to the arrival of the electrical stimulation demonstrated by the novel echocardiography developed in the present study with a high temporal resolution of 2 ms shows great potential for noninvasive assessment of myocardial tissue damage due to heart failure and desynchronization due to fibrillation.

Acknowledgment

The author is grateful to Prof. Emeritus Motonao Tanaka and Prof. Yoshifumi Saijo of Tohoku University for useful discussions. The author also acknowledges the experimental contributions of Assoc. Prof. Hideyuki Hasegawa. The study was approved by the review committee of the Graduate School of Engineering, Tohoku University and the healthy subjects

gave informed consent. This study was partly supported by a grant-in-aid for scientific research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan [20360181].

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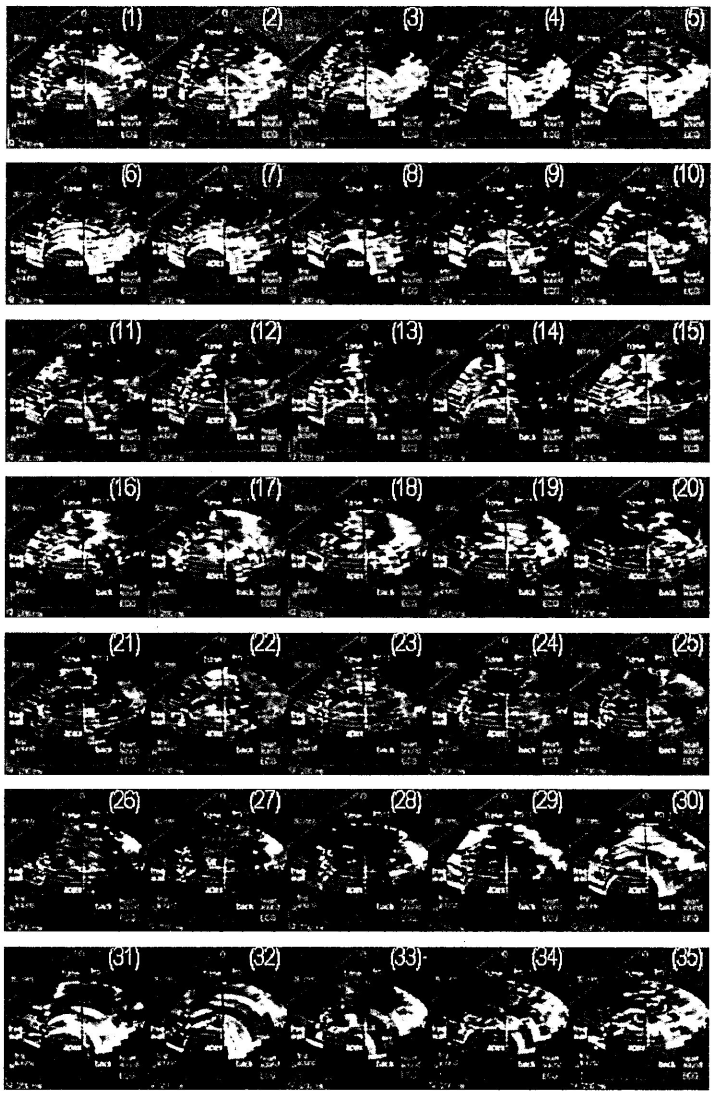

Figure 1(1)-(35). For subject A, 3D visualization of the phase distribution of 40-Hz component of the velocity waveforms at every 5.5 ms.

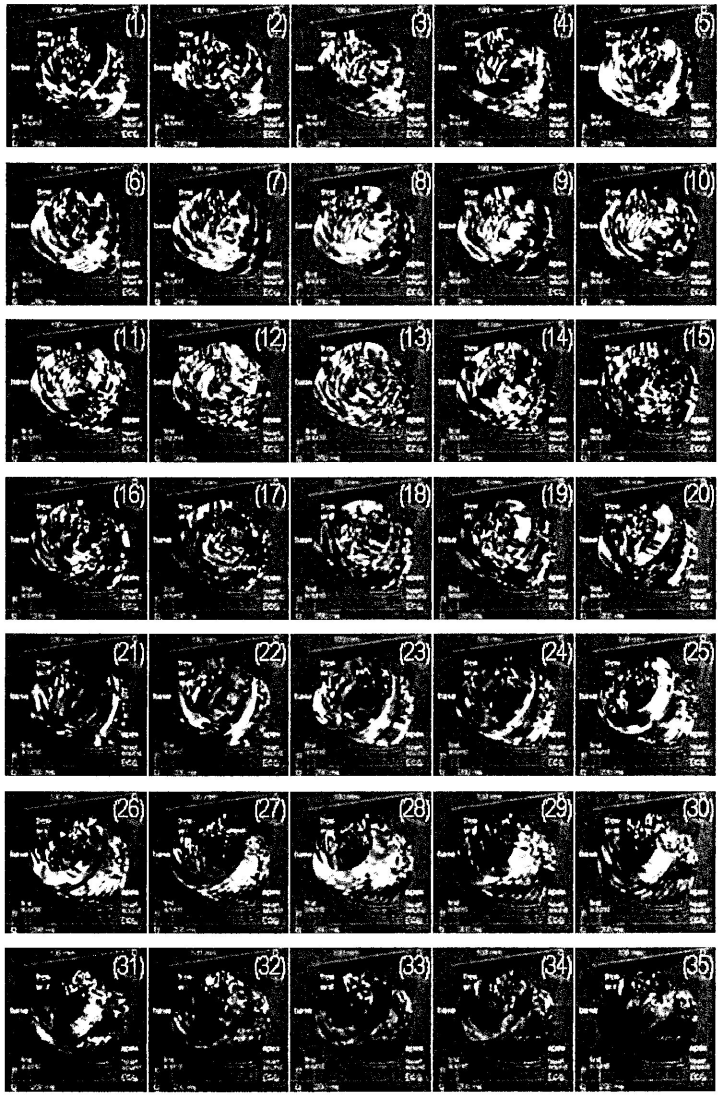

Figure 2(1)-(33). For subject B, the results of the 27-Hz component at every 7.0 ms.

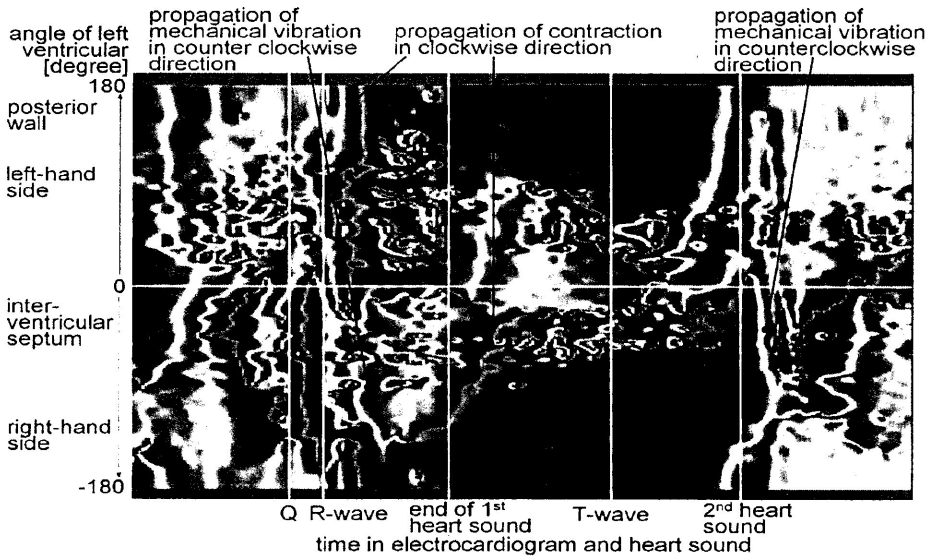

Figure 3. The instantaneous distribution of the phase on the short-axis plane was rearranged along the circumferential direction and set in an array consecutively at every 2 ms from the time of P-wave of the ECG, precisely revealing the propagation of the velocity components in the LV circumferential direction.