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Visualization of Delay Distribution of Myocardial Contraction Response by Electrical Excitation in *in Vitro* Experiments

in vitro 実験における電気的興奮に伴う心筋応答の遅延分布の可視化

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1. Introduction

About 7.3 million people in the world and 20 thousand people in Japan die of heart disease in a year[1), 2)]. Our study group focused on delay time of myocardial contraction in response to conduction of action potentials arising from the sinoatrial node. To realize *noninvasive* detection of such minute myocardial responses to the propagation of the action potential in the human heart[3)], it is necessary to examine temporal relationship from electric excitation to myocardial contraction. In the present study, we measured the spatial distribution of myocardial contraction in response to electrical stimulation *in vitro* using ultrasound.

2. *In Vitro* Experimeantal System

As illustrated in **Fig. 1**, we designed an *in vitro* experiment system to measure vibration velocity $v(t)$ of the myocardial contraction in response to an electrical stimulation. Ultrasonic RF data were acquired using a 10 MHz linear probe of ultrasonic diagnostic equipment (Aloka α-10). The sampling frequency of the RF signal was 40 MHz. An specimen was the left ventricular wall which was isolated from the heart of Sprague-Dawley rat. Krebs-Henseleit solution was circulated in the water tank, which was kept constant at 37 degrees Celsius. Mixed gas (O_2 95%, CO_2 5%) was melted into the solution. Repetition frequency and amplitude of the electric stimulator were 2 Hz and 3 V, respectively.

3. Principle

3.1 Parallel Beam Forming

To realize a high temporal resolution, parallel beam forming[4)] was employed. In the present study, the number of transmissions was 3,and 72 receiving beams were obtained for 3 transmissions. As a result, a high frame rate $(1/\Delta T)$ of 3472 Hz was realized to measure the delay time of myocardial contraction in response to electrical stimulation, which is expected to be several m/s.

3.2 Phased-Tracking Method

We measure vibration velocity $v(t)$ caused by contraction on 72 points along the myocardium of rat with intervals of 0.2 mm using the phased-tracking method[5)]. The average velocity $v(t + \Delta T/2)$ of an object during the transmission interval ΔT of ultrasound pulses is accurately estimated using the phase shift in the received ultrasonic pulses as follows:

$$v\left(t + \frac{\Delta T}{2}\right) = c_0 \frac{\Delta\theta(x;t)}{4\pi f_0 \Delta T}, \qquad (1)$$

where c_0 is the velocity of ultrasound, f_0 is the center frequency, $\Delta\theta(x;t)$ is the phase shift of the received ultrasound signal during ΔT.

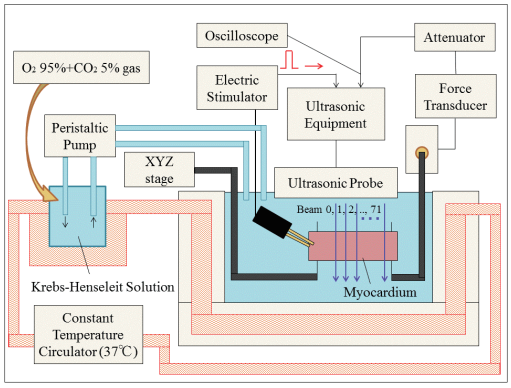

Fig. 1 Schematic diagram of the experimental system.

4. Apparent Propagation Velocity of Contraction

Apparent propagation velocity of contraction c_s was calculated from the delay time τ of velocity

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$v_j(t)$ in beam j from that $v_i(t)$ in beam i and the distance Δd_{ij} between beams i and j. Delay time τ_j was calculated by cross-correlation functions (CCF) $\tau_{i,j}$ between $v_i(t)$ and $v_j(t)$ as follows:

$$r_{ij}(m) = \frac{1}{\sigma_i \sigma_j N} \sum_{n=0}^{N-1} (v_i(n) - \overline{v_i})(v_j(n+m) - \overline{v_j}) \quad (2)$$

where σ_i and σ_j are the standard deviation of $v_i(n)$ and $v_j(n)$, $\overline{v_i}$ and $\overline{v_j}$ is average velocity, n is the frame number, and m is the number of lag samples. We calculated all the delay times $\tau_{1\sim71}$ using the CCF. Propagation velocity c_s was determined by the least-squares fitting to the slope of the relationship between τ and Δd_{ij}.

In the present study, myocardial contraction in response to electrical excitation was visualized by mapping delay time of velocity waveforms.

5. Results

5.1 Measurement of $v(t)$ and Calculation of c_s

Electric stimulation signal, vibration velocity waveforms $v_{45}(t)$ and $v_{55}(t)$ and tensile force are shown in **Fig. 2**. The generation of tensile force and muscle contraction were accompanied by the electrical stimulation. A low-pass filter with a Hanning window (window length: 1.44 ms) was applied to each velocity waveform to cut high-frequency noise (cutoff frequency: 700 Hz).

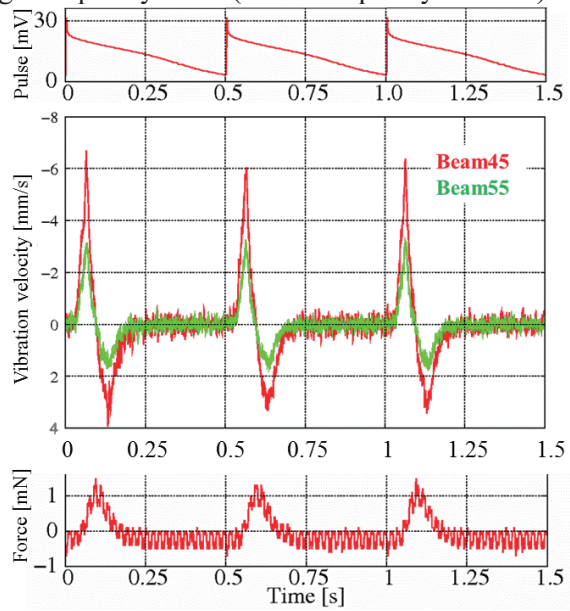

Fig. 2 Electric stimulation (upper), vibration velocity waveforms measured at beam positions of 45 and 55 (middle), and tensile force between both sides (bottom).

Using the slope value in **Fig. 3**, apparent propagation velocity of myocardial contraction c_s was estimated to be 1.4 m/s.

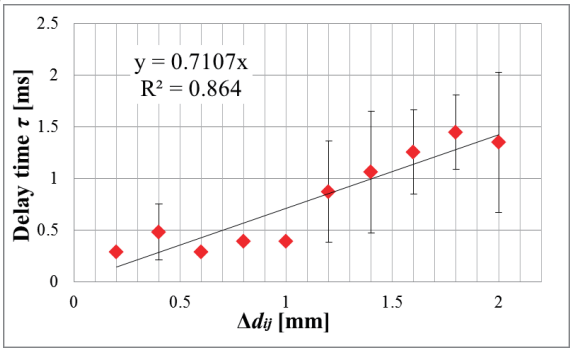

Fig. 3 Delay time of vibration velocity at each beam from that at Beam 45.

5.2 Visualization of Delay Time Distribution of Myocardial Contraction Response

Delay time distribution of myocardial contraction response from beam 45 at surface (=depth 0 mm) is shown **Fig. 4**. Propagation of contraction can be seen from beam 45 (=distance 0 mm) to beam 55 (=distance 2.0 mm).

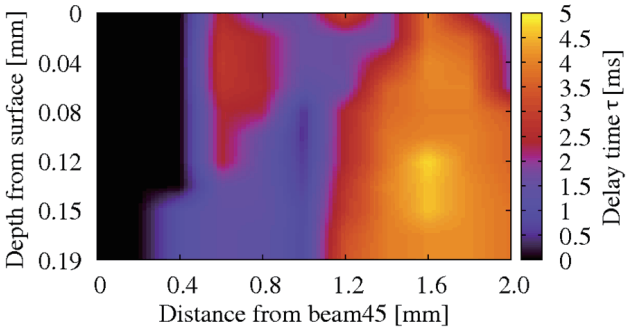

Fig.4 Delay time distribution against beam 45 at surface (= depth 0 mm).

6. Conclusion

In this study, we could estimate apparent propagation of myocardial contraction c_s and visualize delay time distribution of myocardial contraction response.

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