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● *Technical Note*

STRAIN RATE DISTRIBUTION IN LAYERED MYOCARDIUM MEASURED USING LOCAL VELOCITY ESTIMATOR WITH MULTIFREQUENCY PHASE DIFFERENCES

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Abstract—Measurement of the myocardial strain rate (SR), with high spatial resolution, is useful in evaluation of the transmurality of myocardial infarction. As the SR distribution is calculated using velocities observed at multiple positions in the heart wall, it is necessary to estimate the local velocity to measure SR distribution. In the present study, our previously proposed local velocity estimator, with multifrequency phase differences, was used to measure SR distribution in the heart wall. The SR distribution measured with the proposed local velocity estimator revealed alternate layers of contraction and relaxation, which were not measured with the conventional velocity estimator with spatial averaging. The reproducibility of the SR distributions was confirmed in three consecutive heartbeats with three subjects. High-spatial-resolution SR measurement with the proposed local velocity estimator will allow myocardial layer-specific analysis in the transmural direction. (E-mail: mori@ecei.tohoku.ac.jp)

Key Words: **Ultrasound, Heart wall, Strain rate, Layered myocardium, Phase difference.**

INTRODUCTION

Ultrasound-based measurements of myocardial strain rate (SR) have been studied to evaluate regional myocardial function. The regional SR is useful for defining the transmurality of myocardial infarction (Weidemann et al. 2003). Myocardial layer-specific analysis has been conducted to detect myocardial infarction in very early stages (Norum et al., 2015; Rimbaş et al. 2020). Therefore, high-spatial-resolution SR measurement has the potential to detect local abnormalities in the transmural direction.

In previous studies, myocardial SR distributions were measured using ultrasound (Sutherland et al. 2004; Tanaka et al. 2014). As the SR distribution is calculated using the velocities at multiple positions in the heart wall, it is important to estimate local velocities for SR measurement with high spatial resolution. However, ultrasound-based velocity estimators typically require spatial and/or temporal windows for averaging (Kanai et al. 1997).

In a previous study, we proposed a velocity estimator, with multifrequency phase differences, to estimate the local velocity without spatial averaging (Obara et al. 2021). As this velocity estimator could alleviate the negative effects of the attenuation in propagation in the living tissue and the interference caused by the superposition of backscattered waves from multiple myocardial fibers, the local velocity in the heart wall was measured without a window for averaging (Obara et al. 2021). The precision of the local velocity estimation was confirmed, and the usefulness for measuring the myocardial SR distribution was discussed in that study. However, this velocity estimator has not yet been applied to the measurements of SR distribution.

In the present study, the myocardial SR distribution in the transmural direction for healthy subjects was measured using the conventional velocity estimator, with a single-frequency phase difference, and the proposed velocity estimator, with multifrequency phase differences. To discuss the relationship between the locality of the velocity estimation and the SR distribution in the transmural direction, we compared the spatial distributions of SR measured using a velocity estimator without spatial averaging and those with spatial averaging.

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METHODS

Subjects

Three healthy subjects aged between 20 and 29 agreed to participate in this study. The human study protocol was approved by the ethics committee of Tohoku University, and the individuals agreed to participate in this study.

Ultrasound data acquisition

In vivo measurements were applied to the interventricular septum (IVS) in the parasternal long-axis view (Fig. 1a) using an ultrasound diagnostic apparatus. Focused waves with a center frequency, f_c, of 3.75 MHz were transmitted from a sector probe (UST-160 52101; Hitachi-Aloka-Medical Ltd., Tokyo, Japan) connected to an ultrasonic diagnostic apparatus (SSD 6500; Hitachi-Aloka-Medical Ltd.). The sampling frequency, f_s, was 20 MHz. The interval between the sample points was 0.038 mm, assuming that the sound velocity in living tissue is 1540 m/s.

A previous study measuring the myocardial SR distribution focused on the propagation of contraction caused by the conduction of electrical excitation (Yoshiara et al. 2007). Considering that the conduction speed of electrical excitation in the vertical direction of the myocardial fiber, that is, the transmural direction of the heart wall, is 80−200 mm/s (Sano et al. 1959), the frame rates, f_{FR}, were set at 630 Hz for subjects A and B and 425 Hz for subject C by reducing the number of ultrasound beams in acquiring the ultrasound data.

Physiological data acquisition

For each subject, the electrocardiogram (ECG) waveform was measured for lead II using the three-point lead method. The phonocardiogram (PCG) waveform was measured simultaneously using a small microphone attached to the subject's chest.

Measurement of myocardial SR distribution

In the present study, the measurement of the myocardial SR distribution was applied to the time phase around the R-wave in the ECG, which is associated with the onset of the myocardial contraction. The region of the IVS was manually segmented, and the radiofrequency data on the beam that was parallel to the transmural direction of the IVS were analyzed (Fig. 1a). The analysis was processed offline using our own developed software on a Linux system.

The conventional velocity estimator, with a single-frequency phase difference (Kanai et al. 1997), and our previously proposed velocity estimator, with multifrequency phase differences (Obara et al. 2021), were applied to radiofrequency data to estimate the velocities at multiple positions on the heart wall. In the conventional velocity estimator, the spatial averaging by the cross-correlation function was needed to alleviate the negative effects of the attenuation in propagation in the living tissue and the interference caused by the superposition of backscattered waves from multiple myocardial fibers. Our previously proposed velocity estimator does not require the spatial averaging operation because this estimator can alleviate these negative effects using multifrequency phase differences weighted by the amplitude

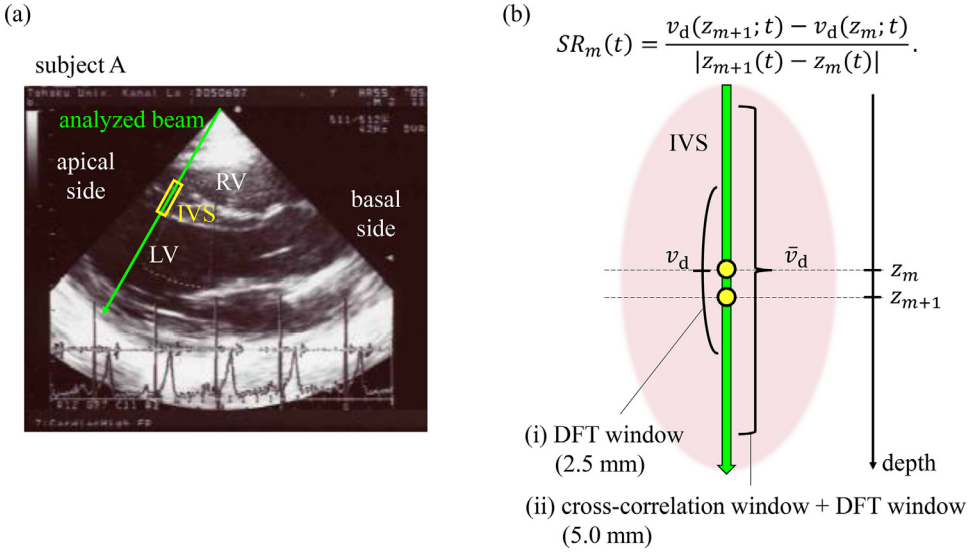

Fig. 1. (a) B-mode image of the cross-section where the ultrasound data were acquired in the parasternal long-axis view. (b) Schematic of the measurement of myocardial strain rate (SR) distribution. DFT = discrete Fourier transform; IVS = interventricular septum; LV = left ventricle; RV = right ventricle.

of the cross-spectrum between two consecutive frames. The local velocity estimation without spatial averaging is useful to measure the heart wall dynamics where the change in thickness occurs.

In both velocity estimators, the velocities were estimated under two different conditions, as illustrated in Figure 1b. Condition (i) was without spatial averaging by the cross-correlation function. Thus, its window length corresponded to the Hanning window for the discrete Fourier transform (DFT) in the velocity estimation (2.5 mm). Condition (ii) was with spatial averaging by the cross-correlation function (Kanai et al. 1997). The total window length in condition (ii) was 5.0 mm.

The SR distribution was obtained by calculating the SR using the velocities at two positions. The SR at the mth position at time t was calculated as (Tanaka et al. 2014)

$$\mathrm{SR}_m(t) = \frac{v_\mathrm{d}(z_{m+1};t) - v_\mathrm{d}(z_m;t)}{|z_{m+1}(t) - z_m(t)|}. \quad (1)$$

Here, $z_m(t)$ is the depth of the mth position, and $v_\mathrm{d}(z;t)$ is the velocity in the beam direction at depth z. The initial interval $|z_{m+1}(0) - z_m(0)|$ for calculating the SR was 0.82 mm used in a previous study (Tanaka et al. 2014).

Evaluation for reproducibility of SR distribution in layered myocardium

The reproducibility of SR distribution was evaluated around the time of the R-wave in the ECG in three consecutive heartbeats. We calculated the standard deviation (SD) among three consecutive heartbeats in the SR distributions to compare quantitatively the reproducibility in the conventional method with that in the proposed method. The region of interest (ROI) for calculating the SD was set at a region of 40 ms × 5 mm on the mid-IVS on the M-mode image. The SDs among three consecutive heartbeats were calculated for every depth and time (frame) in the ROI, and SDs in the ROI were averaged.

RESULTS

Figure 2a illustrates the M-mode image of the IVS during the time phase around the R-wave in the ECG, where the *yellow lines* represent the tracking points on the right ventricular and left ventricular sides of the IVS.

Figure 2b–e illustrates the SR distribution in the IVS measured using the conventional (single-frequency) and proposed (multifrequency) velocity estimators. The positive and negative SRs measured in the parasternal long-axis view indicated the increase and decrease in the thickness of the cross-fiber direction, respectively. Considering the volume conservation law, the increase (decrease) in the thickness indicated the contraction (relaxation) of the myocardial fiber. In Figure 2b–e, the cold (warm) color represents the increase (decrease) in the thickness, indicating contraction (relaxation).

The SR distributions, measured using the velocity estimators without spatial averaging, reveal alternate layers of contraction and relaxation, as shown in

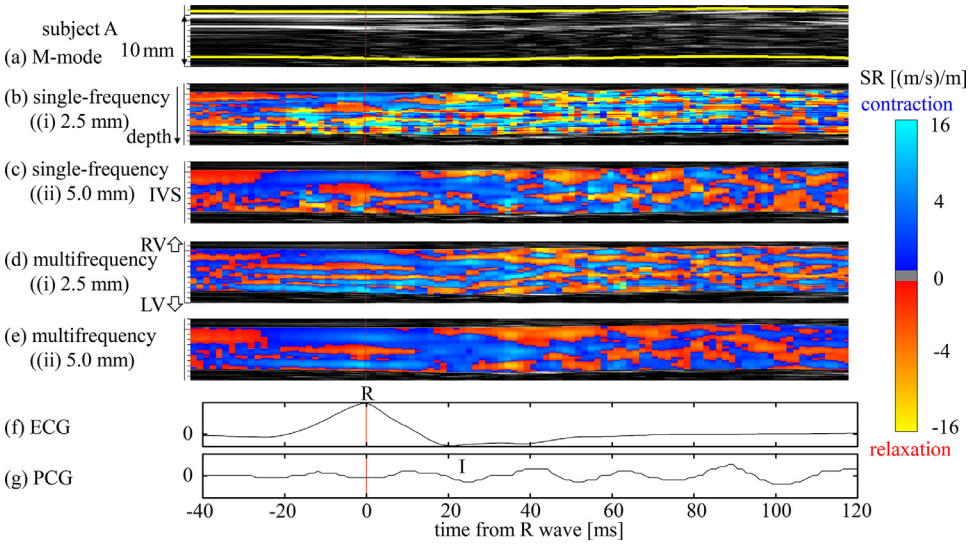

Fig. 2. (a) M-mode image of the interventricular septum (IVS). (b) Strain rate (SR) distribution measured with the conventional velocity estimator, using a single-frequency phase difference, without spatial averaging. (c) SR distribution measured using the conventional velocity estimator with spatial averaging. (d) SR distribution measured with the proposed velocity estimator, using multifrequency phase differences, without spatial averaging. (e) SR distribution measured with the proposed velocity estimator with spatial averaging. (f) Electrocardiogram (ECG) waveform. (g) Phonocardiogram (PCG) waveform. LV = left ventricle; RV = right ventricle.

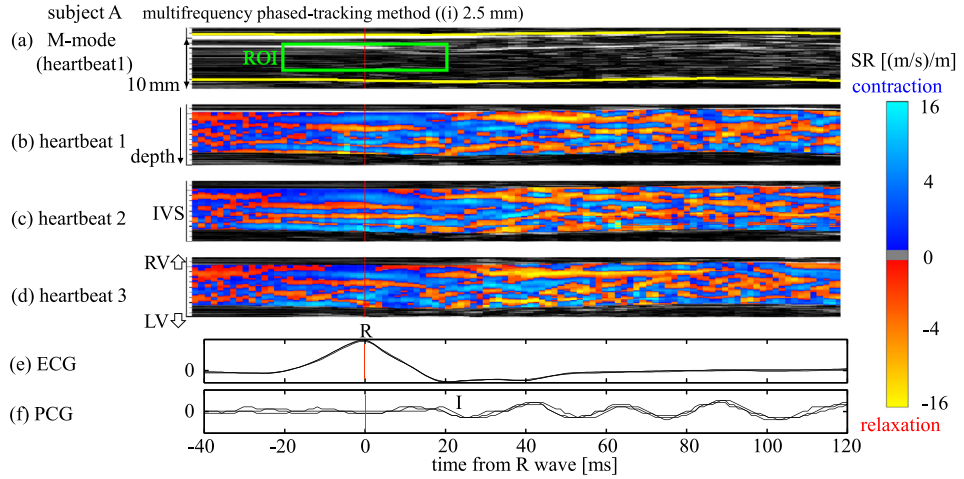

Fig. 3. (a) M-mode image of the interventricular septum (IVS) in heartbeat 1. (b–d) Strain rate (SR) distributions measured using the proposed velocity estimator without spatial averaging for (b) heartbeat 1, (c) heartbeat 2, and (d) heartbeat 3, respectively. (e) Electrocardiogram (ECG) waveform. (f) Phonocardiogram (PCG) waveform. LV = left ventricle; ROI = region of interest for calculating the averaged standard deviation in the SR distributions; RV = right ventricle.

Figure 2b, 2d. Although no temporal window was used for averaging, this multilayered pattern of the SR distribution measured by the proposed local velocity estimator was continuous between the rising time of the R-wave in the ECG and the rising time of the first heart sound in the PCG, which represented the start of the ejection phase (Fig. 2d). In the velocity estimators with spatial averaging, this multilayered pattern did not appear, as shown in Figure 2c, 2e, similarly to the previous study using the conventional velocity estimator with spatial averaging (Tanaka et al. 2014).

The reproducibility of the SR distribution measured using the conventional and proposed velocity estimators without spatial averaging was evaluated in three consecutive heartbeats for three healthy subjects. Figure 3 illustrates the SR distributions measured by the proposed local velocity estimator for subject A for three consecutive heartbeats. The values of averaged SDs among three

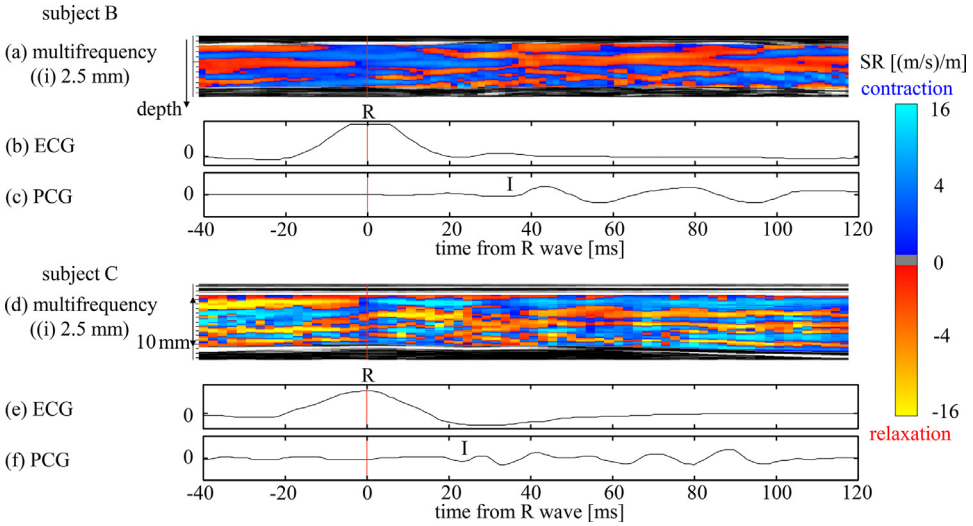

Fig. 4. (a) Strain rate (SR) distribution measured using the proposed velocity estimator without spatial averaging for subject B. (b) Electrocardiogram (ECG) waveform for subject B. (c) Phonocardiogram (PCG) waveform for subject B. (d) SR distribution measured using the proposed velocity estimator without spatial averaging for subject C. (e) ECG waveform for subject C. (f) PCG waveform for subject C.

consecutive heartbeats in the SR distributions were 8.4 (conventional method) and 1.9 (proposed method) in subject A. Figure 4 illustrates the SR distributions for subjects B and C. The values of the averaged SDs were 5.8 (conventional method) and 1.2 (proposed method) in subject B and 9.2 (conventional method) and 3.7 (proposed method) in subject C. In three subjects, the values of the averaged SD in the proposed method were smaller than those in the conventional method. Therefore, the proposed method was more reproducible than the conventional method.

DISCUSSION

We discussed the relationship between the locality of the velocity estimation and the multilayered pattern of the SR distribution. As shown in Figure 2, the multilayered pattern of SR distribution was measured using a velocity estimator without spatial averaging and was not measured using that with spatial averaging. The velocities in the heart wall contain the large velocity caused by the whole motion of the heart wall and the minute velocity caused by the change in the local myocardial layer thickness. In averaging the velocities spatially, the local and minute changes in thickness may be suppressed as the variance of velocities in the window of the velocity estimation, and the velocity caused by the whole motion of the heart wall is estimated. Thus, the layered pattern, as well as the number and thickness of layers in the SR distribution, might depend on the locality of the velocity estimation. As the calculation of the cross-correlation function causes the spatial averaging operation weighted by the amplitude of the analyzed signal, it is not suitable for the layer-specific analysis in the transmural direction of the heart wall. In previous studies such as the M-mode tissue Doppler imaging technique or the conventional velocity estimator, a single-frequency phase difference was used and more homogeneous SR distributions in the transmural direction were measured (Derumeaux et al. 2000; Tanaka et al. 2008). As these velocity estimators typically require spatial averaging, the homogeneous SR distributions have resulted from the effects caused by the spatial averaging.

As discussed in a previous study, the conventional velocity estimator is affected by the negative effects of the attenuation in propagation in the living tissue and the interference caused by the superposition of backscattered waves from multiple myocardial fibers (Obara et al. 2021). Thus, the averaged SD in the local SR distribution measured using the conventional velocity estimator was large compared with that using the proposed velocity estimator which can alleviate the negative effects. Thus, the proposed velocity estimator with multifrequency phase differences is needed for estimating precisely the local velocity without the cross-correlation function (Obara et al. 2021).

However, it could not be validated whether the reproducibility evaluated by the SD of the SR distribution measured using the proposed method is sufficient or not for *in vivo* measurement, and this is our future work. Moreover, the accuracy of the proposed method has not been evaluated by comparing it with the "true" velocity or SR. The accuracy evaluation allows the discussions about the limitation of locality and the suitable window length for measuring the SR distribution. These concerns will be validated and discussed in our future studies.

High-spatial-resolution SR measurement in the transmural direction using the proposed local velocity estimator applies to the region where the ultrasound beam corresponds to the transmural direction of the heart wall. Thus, the measurement view is limited depending on the region of the heart to set the ultrasound beam direction along the transmural direction.

In the present study, high-spatial-resolution SR measurement in the transmural direction was used in healthy subjects. The SR distribution measurement for an abnormal subject and the comparison of the result with that in the healthy subject may allow discussion of the relationship between the alternate layers of contraction and relaxation with the electromechanical and physiological mechanism of the heart. Elucidation of the physiological role of the alternate layers is important to determine whether these layers are related to the actual contractile response of the layered myocardium or not. It is our future work to measure the SR distribution of an abnormal subject.

CONCLUSIONS

To measure the myocardial SR distribution with high spatial resolution in the transmural direction, the proposed local velocity estimator was applied to the measurements of SR distribution. The local measurement using the proposed velocity estimator with multifrequency phase differences was more reproducible than that using the conventional velocity estimator with a single-frequency phase difference. The SR distribution revealing alternate layers of contraction and relaxation was observed in the proposed method by improving the locality of the velocity estimation. High-spatial-resolution SR measurement using the proposed local velocity estimator will allow myocardial layer-specific analysis in the transmural direction.

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Conflict of interest disclosure—The authors declare that they have no competing interests.

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