Historical Perspective of the Development of Diagnostic Ultrasound in Cardiology

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***Abstract*—The diagnostic application of ultrasound in clinical medicine advanced uniquely in the field of cardiology. The cardiovascular system is a most suitable organ for the application of ultrasound for use in obtaining information regarding structure and function, which are difficult to obtain using other diagnostic methods and which are indispensable for accurate diagnosis of diseases.**

However, because of the complicated structure and characteristics of the functioning of the heart, unique and creative technologies had to be developed for practical applications.

In this paper, perspectives of the historical development of ultrasonic diagnostic technology, which originated as key elements for improving clinical cardiology and which developed in our laboratory, are systematically presented. First, as the most important affair in the first step of clinical application of ultrasound, the introduction and establishment of the practical use of the focused ultrasound to the ultrasonic pulse reflection method are described. Next, we address two-dimensional echocardiography and its related technology such as tomo-kymography, combination of M-mode method, Doppler method, and tomography etc. Then we discuss ultrasonic tissue characterization in cardiology by echo method and the development and application of ultrasonic microscopy for biomedical use. We address modulated ultrasonic Doppler method including the two-dimensional Doppler method. Finally, after introducing the data processing technique, we conclude with new technology for deducing the functional information on cardiovascular function, such as contractility of the local myocardium, local flow volume, and local pressure in the heart chambers and their two-dimensional distribution, which are very important for accurate estimation of the heart function.

I. Introduction

In clinical medicine, detailed information on the morphological and physiological changes of organs is indispensable for accurate diagnoses of diseases. To obtain such information easily in a non-invasive manner, ultrasonic diagnostic techniques for displaying the structure and function of tissues and organs were developed in the fifth to sixth decade of the 20th century [1]–[5].

Three basic techniques were developed for the practical application of ultrasound in the field of clinical cardiology. The first, M-mode echocardiography, which is also called the time-position indication method [6], used the pulse reflection technique developed by Edler and Hertz in 1954 [7]. The second, the ultrasonic Doppler method employed for the measurement of the motion of the reflector, such as blood or a cardiac structure, was developed by Satomura and Nimura in 1956 [8], [9]. The third, two-dimensional echocardiography, termed the ultrasonocardio-tomography, was developed by Tanaka et al. in 1964 [10]–[12]. Two-dimensional display of structure and function information was the essential technique for clinical diagnosis, because of the following advantages. First, an anatomical site, i.e., a target object, in a pathological state or critical condition can be identified accurately spatially with ease. Second, intuitive estimates of abnormalities occurring in the organ can be made safely with ease and in real time. Accordingly, studies of the ultrasonic imaging of a human body in two dimensions were begun by several investigators in the sixth decade of this century [1], [3], [13], [14].

However, at that time, only circular plane transducers were used generally in echography. Two-dimensional images were made by echo signals obtained from the organs, during ultrasonic scanning, and displayed on a storage oscilloscope as the integrated images that were overlapped with each echo signal obtained from different beam directions. The resolution of the picture, i.e., quality of the image, was very poor and inadequate for displaying finely detailed structures such as those of the heart.

To develop further ultrasonic applications in cardiology as a diagnostic tool, performance of basic investigations, e.g., analysis of the sound field in the medium, the processing of echo signals, etc., were urgently required. This paper focuses on the work of our laboratory. It is hoped that it provides a coherent and systematic presentation on one approach to the goal of applying ultrasound to clinical cardiology.

II. Introduction of the Sound Field Control Technique to Diagnostic Ultrasound

A. Design of the Ultrasonic Transducer for Obtaining High Quality Echograms

In addition to the medical requirements and engineering problems mentioned previously, the following existing acoustical limitations had to be broken through. According to the anatomical position of the heart and the acoustic characteristics of the thorax and the lung [15], the following points are true: 1) the heart is enveloped by the osseous frame, which greatly limits the ultrasonic scan area on the thorax; 2) the lung, which lies on both sides of the heart, exhibits a very large acoustic attenuation by virtue of the air it contains; 3) the back of thorax contains a

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thick layer of muscle; and 4) the heart pulsates continuously. Accordingly, it had been considered that an ultrasonic two-dimensional picture of the heart was extremely difficult to obtain in the living state without development of more advanced technology.

To solve these anatomical and acoustical problems, it was necessary to develop the following new techniques: 1) control techniques of the radiated sound field, especially a converging technique for making the beam narrower than the size of observed structure components; 2) methods for compensating attenuation of ultrasound along the pathway [15] or methods for increasing the acoustic power of the weak echoes reflected from the target area at remote distances; and 3) control techniques synchronized with ECG signals.

Because few theoretical and experimental studies regarding the spatial distribution of the sound field had been published at that time (late 1950s through early 1960s), Tanaka et al. began to investigate the convergence of sound fields by introducing acoustic lenses and concave transducers in 1963 [16], [17].

Prior to that time, theoretical analyses of the spatial acoustic pressure distribution of the concave transducer were carried out using the two new theories. One was originated by Prof. Y. Torikai (Tokyo University) in 1955 [18], 1960 [19], and 1962 [20]; the other was originated by S. Ohtsuki's ring function in 1972 [21].

These theoretical results were compared with the experimental results of the spatial sound field obtained by measuring the intensity of the echo reflected from a very small spherical target, about 0.3 mm in diameter; the target was moved laterally, in 1-mm intervals in degassed water, in coordination with the echo intensity, thus obtaining a result that was proportional to square of the sound pressure at the target [17]. The theoretical results compared well with the experimental results particularly because of the improvement of the azimuthal resolving power attributable to the narrow beamwidth from the converging effect [16], [17].

With the use of Torikai's theory [20], with the concave transducer in the ultrasonic reflection technique, Tanaka proposed that better results should follow with the use of a transducer having the following configuration [17]:

$$R^2/(A\lambda) \leq 4$$

where R is the transducer radius, A is radius of curvature, and λ is the wavelength in the medium.

Tanaka et al. pointed out that the following favorable effects were obtained by employing the transducer of this configuration [17].

- The beam width could be made sufficiently narrow so that local selectivity was markedly improved, providing obtainable high resolution and high quality images.
- The length of the Fresnel' interference zone was made shorter than that of a plane circular transducer of the same size, suppressing the near field relatively such that the proximity immersed method, or direct contact method, could be applied easily.
- The acoustic power converged so that intensified echo signals were readily obtained even in the far distance area.
- The miniaturization of the transducer and the introduction of the STC circuit were made easier.

The satisfactory effects of using the concave transducer appeared markedly in the image quality of the actual tomogram of the heart taken by an immersion method, as shown in Fig. 1. The miniaturization of the transducer made it possible to perform an intracavitary ultrasonic scan, such as transesophageal scan, etc. [22]. Since then, the converged sound field produced by the dynamic focusing method of the annular or phased arrays has been used widely in practical echo machines for diagnostic purposes [49]. Additionally, these converging effects of the sound field of the acoustic lens were applied to the acoustic microscope in 1982 [41], [42].

III. Introduction of the Processing Technique to the Echo Signals

After building up the basis of two-dimensional echocardiography to improve the quality of the cross-sectional image, development and introduction of new technology, such as sensitivity time control (STC) [23], fast time constant (FTC) [24], logarithmic amplifier, improvement for the scanning speed and miniaturization of ultrasonic scanner [22], [25], and ECG-triggered control method [26], were carried out [27]. Thus, Tanaka et al. were the first to obtain high quality cross-sectional images of the heart by mechanical sector scanning in 1965 [27].

IV. Development of Ultrasonic Technology for Obtaining Information on Morphological Changes in Cardiology

A. Macroscopic Dimension Measurement

To increase the accuracy of morphological measurement of macroscopic cardiac structures, the principle of combining two-dimensional echocardiography and M-mode display was proposed in 1965 [28], [29] (Fig. 2). Thus, in 1970, various features of cardiac structures, such as thickness of the heart and vessel wall, internal and external diameter of the chambers, size and shape of the cardiac structure, localized deformity etc., could be estimated on the ultrasonic cross-section image [29], [30]. However, two basic problems remained: the measurement of the thickness and hardness of thin tissue, such as valve tissue and vessel wall [31], and tissue characterization of the myocardium and other heart and vessel tissues.

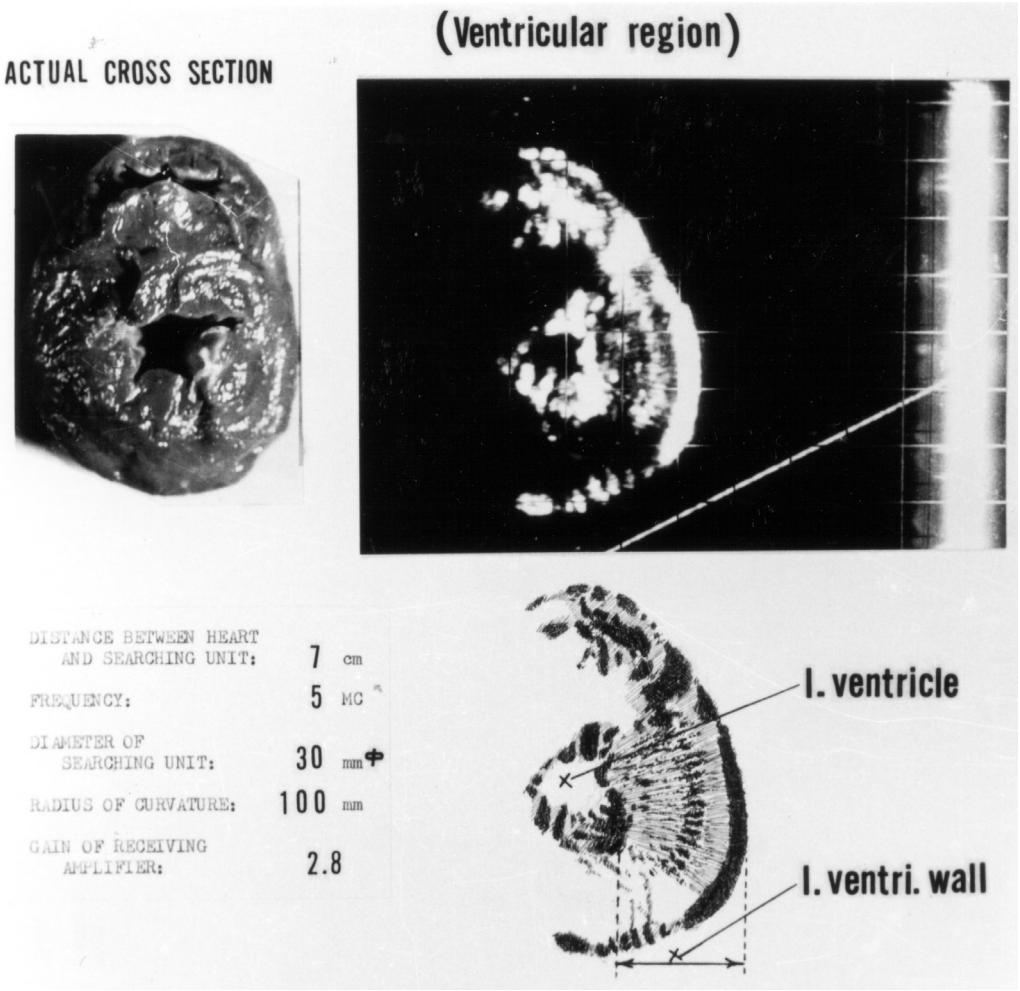

Fig. 1. High quality ultrasono-cardiotomogram (2-dimensional echocardiogram) of a canine heart at the left ventricular level obtained by using a concave disk transducer of 30 mm diameter, 100 mm radius of curvature, and 5-MHZ frequency. The heart just after excision was suspended at the focal area in the water bath. The echo pattern shows the three-layer structure.

B. Measurement of the Thickness and Sound Speed of Thin Tissues

When an ultrasonic pulse impinges on a biological specimen placed in a medium for which the speed of sound is known, two reflected pulse signals from the front and the back surfaces of the specimen are produced as shown in the Fig. 3. In the following, the speed of sound of the immersing medium is Co, the thickness of the specimen is d, the transit time of the ultrasound passing through the immersing medium the same distance as the thickness of the specimen is t_{wd}, the speed of sound of the specimen is C, the transmitting time passing through the specimen is t_{sd}, and the thickness of the specimen is d [31], [32]:

$$\begin{aligned} d = C \times t_{sd} &= Co \times t_{wd} \\ &= Co \times (t_{sd-\Delta t}) \end{aligned}$$

where $\Delta t \equiv t_{sd-twd}$. Therefore, $C = Co\ (1 - \Delta t/t_{sd})$.

Here, when the two reflected signals returned from the front and the back surface of the specimen are obtained, if the thickness of a tissue specimen of interest is more than the wave train length, the two reflected signals are separated, and tsd can be measured easily by using the pulse echo method. However, if the thickness of the specimen is less than about one-half of the wave train length, the two reflected signals are not separable, and tsd cannot be measured.

Then, a new measuring method, in which sound speed and thickness of the thin tissue specimen can be estimated by analyzing the echo signals in the frequency domain, was developed and introduced to clinical cardiology and tissue characterization [31]–[33]. In this case, for the accurate measurement of the t_{sd}, the two reflected signals from the front and the back surface of the specimen are received at the same time and mixed with each other.

When the received signal thus obtained, in which the interference is included, is analyzed in the frequency domain by the FFT method, from the interval between two successive peaks of the frequency spectrum, t_{sd} was accurately estimated.

On the other hand, the time difference (Δt) between two reflected signals, the signal reflected from the bottom behind the inserted specimen (t_{sd}) and the signal from the

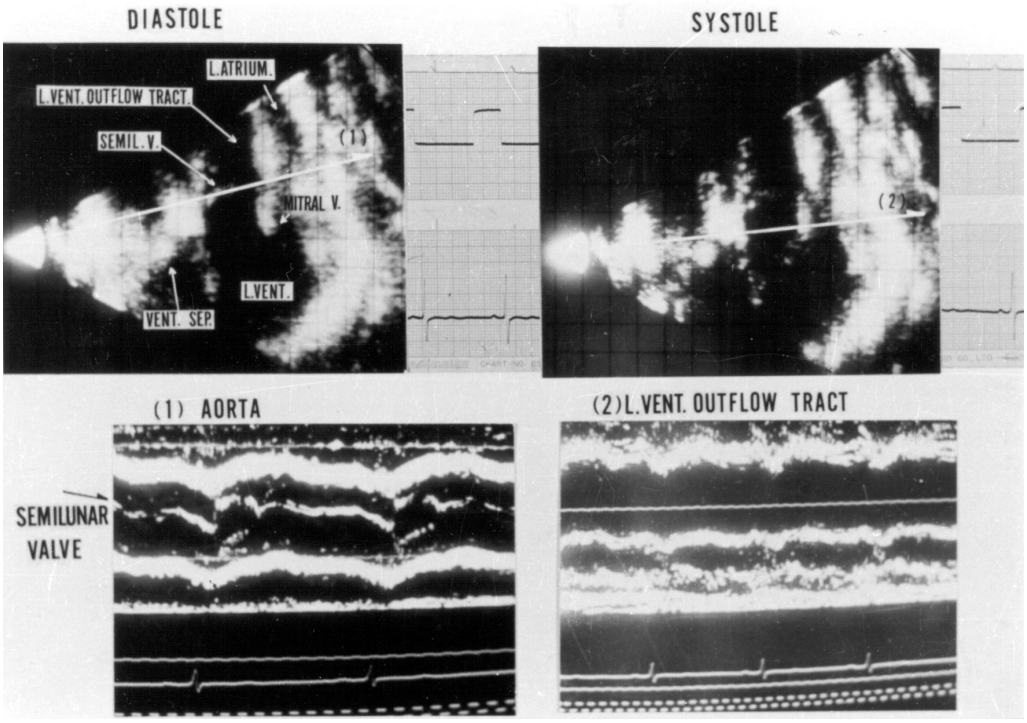

Fig. 2. The M-mode and 2-dimensional echocardiograms obtained by the combination method. The target was the aortic valve and the LV outflow tract area. The aortic valve movement was caught for the first time by this method in 1965. White arrows on the tomograms show the ultrasonic beam direction for obtaining the M-mode image.

bottom without the specimen (t_{wd}), is obtained from the phase difference between both signals, which is the result of analysis in the frequency domain. Thus, the thickness of the thin tissue below the pulse length and the speed of sound passing through the thin tissue were possible to measure accurately by a non-contact and non-invasive method. The value of ultrasonic applications in cardiology was increased.

C. Macroscopic Tissue Characterization in Cardiology

In 1965, when an excised heart was scanned with the compound scanner, using 5-MHz focused ultrasound, it was found that the echogram of the ventricular wall was rather consistent with the actual cross-section of the wall and clearly exhibited the three-layer muscle structure [10]–[12] (Fig. 1). These findings strongly suggested that non-invasive evaluation of changes in myocardial tissue character in myocardial diseases could be performed.

Since then, Tanaka et al. began investigations of ultrasound tissue characterization. In 1970, as a result of clinical research, Tanaka et al. pointed out that when high quality diagnostic equipment was employed in the clinical examination of patients with myocardial damage, such as cardiomyopathy, myocardial infarction, and so on, intensified abnormal echoes from the damaged myocardial area could be frequently detected [30], which they classified into three major types as shown in Fig. 4 [35]–[37].
The first type is a case with an unusual increment in the intensity of the echo reflected from the endocardium. The second type is a case with a broad and intensified echo of

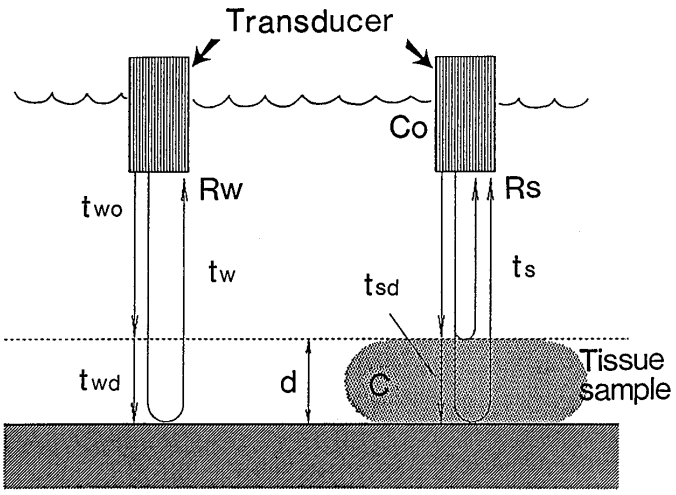

Fig. 3. Schematic representation of the principle measuring method for the thickness and speed of sound for a thin tissue specimen.

the endocardium and a speckle echo localized in the inner half of the myocardium adjacent to the endocardium. The third type has abnormal echoes throughout the myocardium, and the abnormal echoes in the third type were classified into three subtypes of large speckles, medium-sized speckles, and a fine dotted or powder-like pattern as shown in Fig. 5.

Also, the pattern of the myocardial echo changed during one cardiac cycle. In normal cases, myocardial echoes appear throughout the myocardium during diastole and become localized in an area near the endocardium during

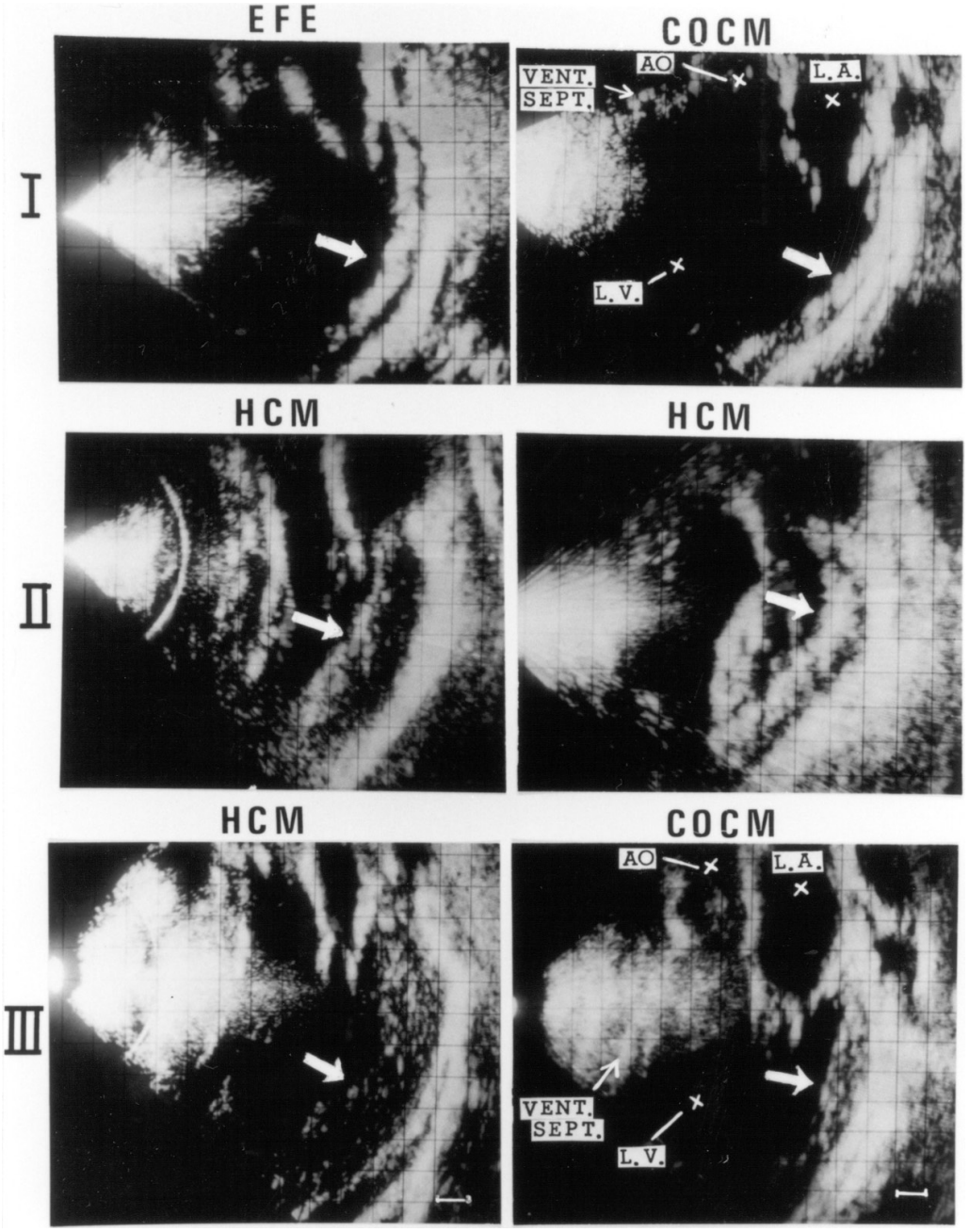

Fig. 4. Three major types of abnormal echo patterns observed with 2-dimensional echocardiograms of the left ventricular wall in cases with the myocardial damage. EFE = Endocardial fibroelastosis, COCM = dilated cardiomyopathy, and HCM = hypertrophic cardiomyopathy. White arrows show the abnormal echo.

systole. The differences of echo intensity between systole and diastole are in the range of 5 to 6 dB in normals. On the contrary, in the case of a damaged myocardium, the pattern of the abnormal myocardial echo shows a small difference or almost no difference between systole and diastole.

On the other hand, a correlation between the echo pattern demonstrated in two-dimensional echocardiogram and actual histological changes of the tissue character were investigated. These showed, for example, that in a case of the first type, a marked degeneration and an increment of fibrous tissue were found in the endocardium and in the surviving myocardial tissue around it. In a case with large speckle echoes in the myocardium and broad strong echoes in the endocardium, thick fibrous tissue and focal degeneration of the myocardium were observed in the endocardium and in its vicinity as shown in Fig. 6.

These facts strongly suggested that the boundaries between the myocardium and the area of degeneration, or of fibrosis, functions as an echo source, and the shape and net-like structure of the fibrotic tissue or localized degeneration tissue would be changed during the cardiac cycle by accompanying contraction and extension of the myocardial fiber [37], [38]. Then, to measure quantitatively the inten-

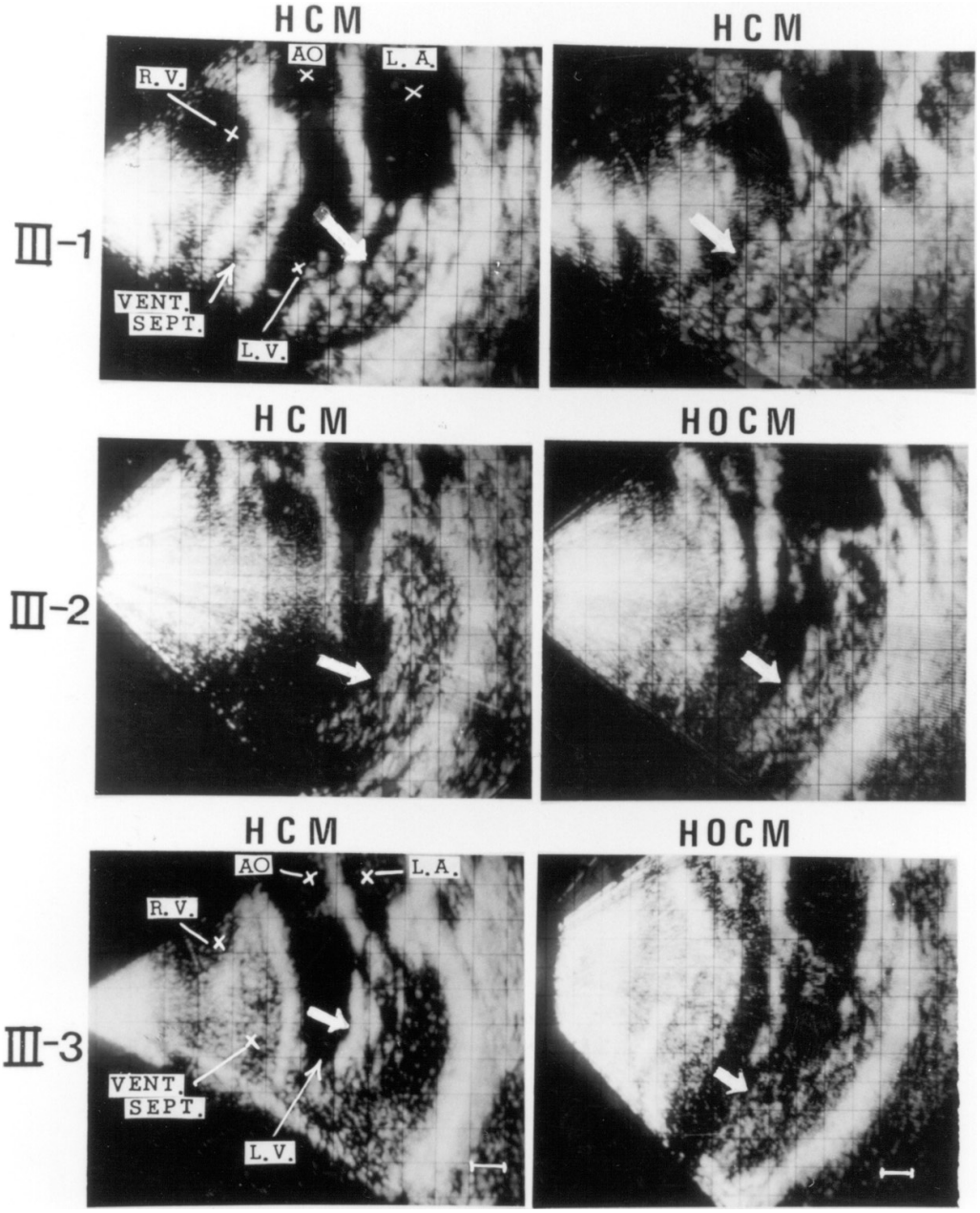

Fig. 5. Three subtypes of echo patterns of speckle observed in the left ventricular wall. HCM = Hypertrophic cardiomyopathy; HOCM = hypertrophic obstructive cardiomyopathy. White arrows show the abnormal speckle echo.

sity of the abnormal speckle echoes, the sensitivity-graded tomogram pair method was developed and introduced in clinical tissue characterization [39]. Using this method, the intensity of abnormal speckle echoes were measured in comparison with that of the echo from the normal pericardium. The intensity of the echo reflected from the scar is approximately 20 dB stronger than that from the normal myocardium. The intensity of the echo reflected from the fibrous tissue is about 5 to 10 dB stronger than that from the normal myocardium [37], [38], [40].

These findings showed that the increment of abnormal tissue produces an increase in the intensity of the abnormal tissue echoes in myocardium and that the grade of pathological fibrotic change in myocardium is possible to estimate non-invasively by using this method in echocardiography [38].

D. Microscopic Tissue Characterization in Cardiology

To develop an understanding of the occurrence of the abnormal echoes and to be able to identify the abnormal tissue in the myocardium on the echocardiogram with accuracy, it was necessary to characterize the normal and abnormal myocardial tissue ultrasonically at the microscopic level. The scanning acoustic microscope (SAM) for the purpose of biomedical application was developed in 1982 [41]; the second one was developed in 1985 at Tanaka's laboratory in collaboration with N. Chubachi (Tohoku Univ. and the HONDA Elect. Co. Ltd.) [38], [42].

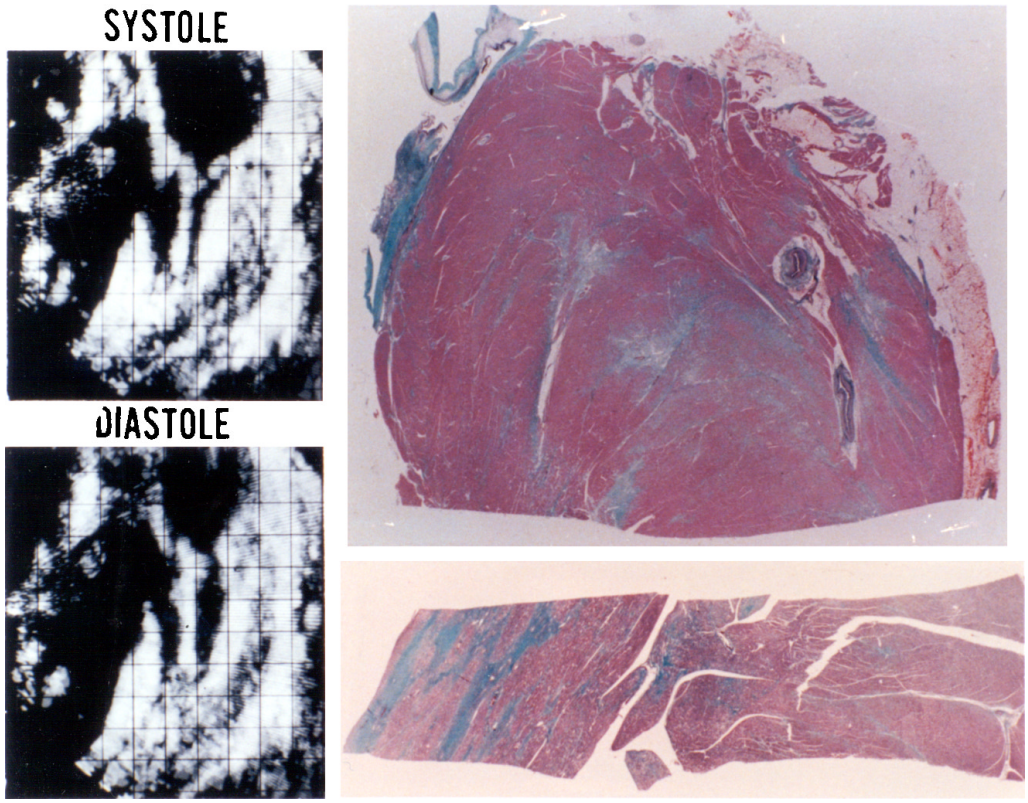

Fig. 6. 2-dimensional echocardiograms of long axis cross-sections of the left ventricle for a case of hypertrophic cardomyopathy and actual cross-section of the ventricle in the same patient taken at autopsy. Histological samples were stained by the Elastica Masson's trichrom stain. The blue area shows the fibrotic tissue.

The diameter of the transducer was about 1.6 mm, and 100- to 200-MHz ultrasound converged through an acoustic lens. The resolution was of the order of 8 μm. The rate of attenuation and the velocity of ultrasound that traveled through the 10-m specimen were quantitatively measured from the two-dimensional pattern displayed on a color CRT by using a two-dimensional high speed scan, the so-called C-scan technique.

The following results were made clear. The velocity of ultrasound in normal myocardium ranges from about 1580 m/s to 1650 m/s. The sound velocity in ischemic tissue of myocardium is slower, and that in the scar tissue faster, than that in the intact myocardium (Fig. 7). Note that, the reflected power at the boundary between the intact myocardium and scar, or fibrous tissue, were calculated from data obtained by using the acoustic microscopic method and compared with the echo intensity obtained in the clinical examination. The values of level differences in reflected power are in good agreement with that of the echo intensity. These results indicated that the boundary between the fibrous tissue and the intact myocardium serves as the echo source. The changes in echo pattern during one cardiac cycle show that the size and spatial arrangement of the boundary between the area of abnormal tissues and normal ones change to a certain extent [37]. It was concluded that the changes of the tissue character, such as degenerative change, fibrotic change, scar, etc., can be evaluated non-invasively by using two-dimensional echocardiography [38]. The possibility of tissue characterization by echo method has also been confirmed by the method of integrated backscatts [43]–[47].

V. Development of Ultrasonic Technology for Obtaining Information on Cardiac Function

The heart is a sacciform organ composed of myocardial fiber and functions as a mechanical hydraulic pump for driving the blood through all parts of the body. When performing the pump function, changes in length of myocardium in the fiber direction, caused by contraction or extension, produces displacement of the chamber wall in the direction perpendicular to the fiber orientation as well as the changes in thickness of the wall. The perpendicular displacement of the wall produces changes in shape, size, and volume of the cardiac chambers. In other words, the force generated by contraction or extension of the myocardium in the fiber direction is converted into force in the direction perpendicular to the fiber by changes in shape and size of the chamber, and this is transmitted to the intracavitary blood. Thus, the blood pressure in the chambers is made to increase in the contraction phase or decrease in the extension phase. The quantity of blood, equal to the volume difference generated by changing the shape and size of the cardiac chambers during the cardiac cycle, is pumped out through the arterial system. Therefore, for the purpose of assessment of cardiac function in

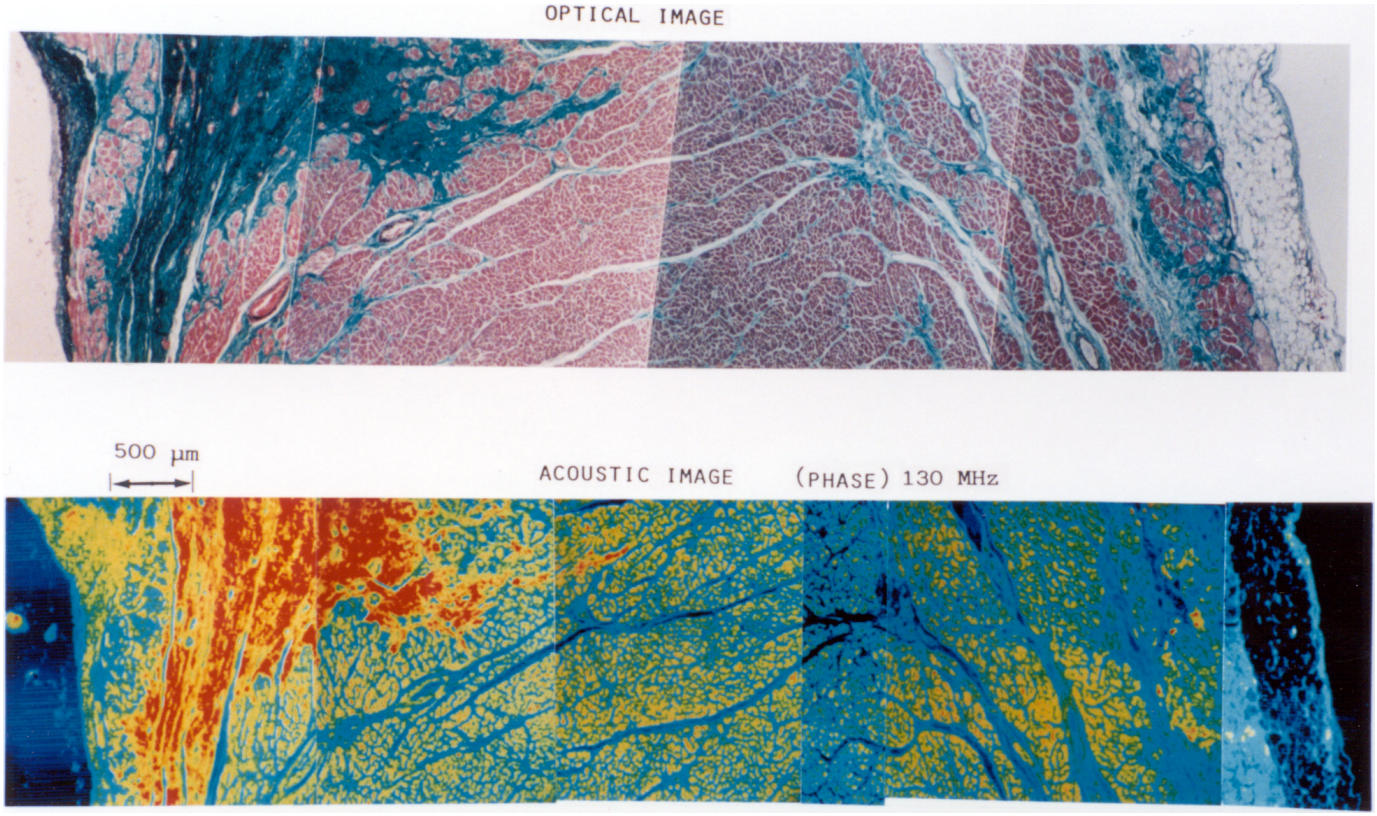

Fig. 7. Acoustical and optical microscopic images of an infarcted myocardium taken from the left ventricular wall in a case with myocardial infarction. In the optical image, the specimen was treated with the Masson's trichrom stain. In the acoustical image, red shows the high speed area, and blue shows low speed area. The intact myocardium is shown in yellow. Ultrasonic frequency used was 130 MHz.

much more detail in the clinic, the following two kinds of functions should be measured in practice: 1) myocardial function, which is the fundamental function of the wall structure of the heart; and 2) hydraulic pump function, which is representative as the deformability of the cardiac structures, changes in the local flow volume and pressure, and their interrelationships during cardiac pulsation.

A. Application of Ultrasound to Measure Myocardial Function

The most common measurements employed to estimate myocardial function are the changes in dimensions of the ventricular wall, such as the displacements of the length of the chamber wall along the longitudinal direction, changes in the circumferential length of the wall at an arbitrary part of the chamber, and changes in velocity and direction of the movement of the wall and the contractile force of a muscle. For this purpose, M-mode echocardiography and two-dimensional echocardiography have been employed frequently. Furthermore, several kinds of application methods mentioned subsequently have been developed by Tanaka et al.

1) Combination Method Using M-Mode Echocardiography and Ultra-Sono-Cardiotomography (1966) [11], [12] (Fig. 2): By using this combination method, the target portion of the cardiac structures to be measured can be easily and precisely confirmed on the cross-section picture of the heart. Moreover, velocity and direction of movements and the magnitude of the displacement of the target portion occurring during the cardiac cycle were measured accurately [48], [49].

2) Ultrasono-Tomokymography (1968) [50] (Fig. 8): By performing the ultrasonic sector scan at a very slow ultrasono-cardiotomography (two-dimensional echocardiography) speed, the image obtained is a two-dimensional echocardiogram on which the amplitude of the motion of various heart structures during the cardiac cycle are superimposed. Accordingly, intuitive observation and measurement of the motion of cardiac structures and of the deformability of the chamber wall can be obtained. Recently this method has been improved as the kinetic imaging method.

3) Development of the Simultaneous Multi-Recording System of M-Mode Echocardiogram, Doppler Echocardiogram, ECG, Phono Cardiogram (PCG), Mechano Cardiogram (MCG), and Pressure Tracing (1970) [51] (Fig. 9): In this system, by using a thermal recording system, the M-mode echocardiogram, and Doppler flow velocity data, it became possible to record these continuously together with physiological data such as ECG, PCG, MCG, and pressure tracing. The interrelationships among the changes in dimension, electrical events, mechanical events, and hydrodynamic events occurring during the cardiac cycle or during disease processes became possible to analyze in de-

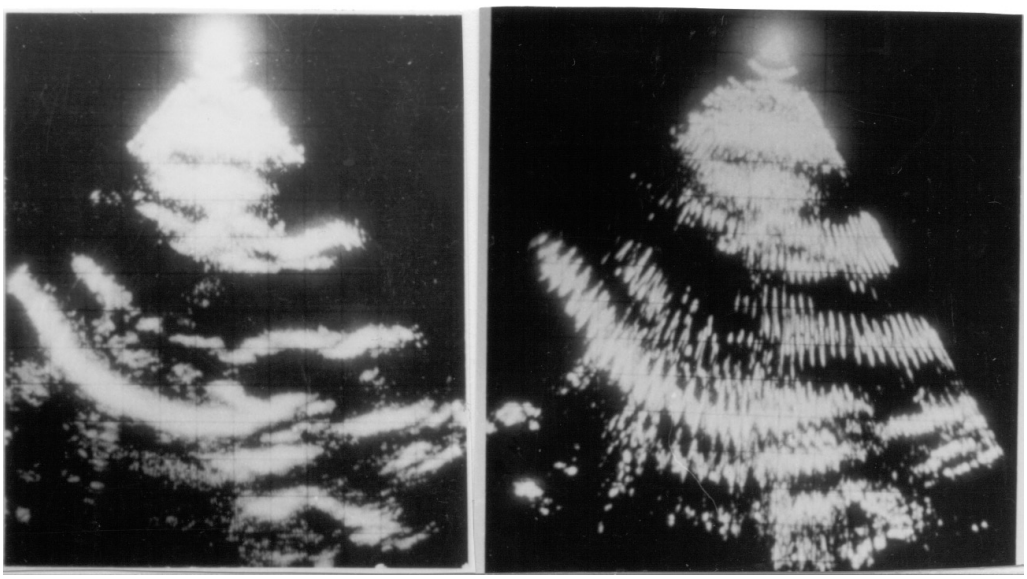

Fig. 8. Ultrasono-tomokymogram (right) and ultrasono-cardio-tomogram (left) for normal hearts.

tail, and following the global functioning of the heart became available [49], [52]–[56].

4) Measurement of the Local Myocardial Function by Development of the Phase Difference Tracking Method (1996) [57] (Fig. 10): For an accurate understanding and estimation of myocardial function (contractility and extensibility) at an arbitrary position in the heart wall, it is necessary to measure changes in thickness of the local myocardial fiber, which is an element of the myocardiam, because the thickness of the myocardial fiber increases in the systolic phase by contraction of the fiber and decreases in the diastolic phase by relaxation of the fiber. However, in the living state, it is difficult to measure the changes in thickness of each myocardial fiber because of a lack of the suitable practical measuring method. Furthermore, the changes in thickness of the fiber are very small (< 10 μm) and are always overlapped with about 10-mm movement of the heart wall, which occurs during one cardiac cycle. Accordingly, for accurate measurement of the myocardial function, the thickness changes of the fiber of < 10 μm have to be measured separately by developing a new method for accurately tracking the large movement of the heart wall.

In 1996, Kanai (Tohoku University) and Tanaka developed and proposed [58], [59] a new method of the "phase difference tracking method" [57] by using the digital data processing technique. In this method, ultrasonic pulse reflection technique is used basically. The phase difference between two successive ultrasonic pulses reflected from a point set arbitrarily in the heart wall is measured. By multiplying the phase difference thus obtained and the velocity of ultrasound in the myocardium, which is approximately 1540 m/s, the moving velocity of the point set in the heart wall that occurred during the time interval between two successive pulses is obtained. Subsequently, when the time integration of the moving velocity during the pulse repetition period is performed, the displacement of the point that occurred during the time interval between two successive pulses is obtained. When the displacement of the point is continuously calculated and recorded using the velocity data obtained from the phase difference between two successive pulse echo signals during one cardiac cycle, the movement of the point in the heart wall including the small amplitude (< 10 μm), which occurred because of changes in thickness of the myocardial fiber, is successfully detected.

On the other hand, when this method is applied to multiple points preset at about every 0.75 mm, i.e., limited with the sampling rate of the A/D converter, in the heart wall along the ultrasonic beam, the spatial distribution of the velocity at these points is obtained simultaneously; the maximum velocity measured is about 0.58 m/s. Then, because of continuous recording of the displacement of each point during the cardiac cycle and the obtaining of differences in the displacement between successive pairs of points, changes in the myocardial layer width thickening can be estimated, as shown in Fig. 10. From knowledge of the layer thickening, regional myocardial functioning, such as strain, strain energy, and movability (contractility and/or extensibility), of the local myocardial fiber could be estimated non-invasively and precisely clinically [60].

B. Application of Ultrasound to Measure the Hydraulic Pump Function of the Heart

The pump function is represented as deformability. Deformability is the capability to make changes in the shape of the heart chamber and the position and configuration of structures such as valve leaflets, chorda tendinea, papillary muscles, chamber wall, etc. Deformability of the heart is affected by the direction and magnitude of the force produced at each local area of the chamber wall and plays an important role to making blood move into and out of

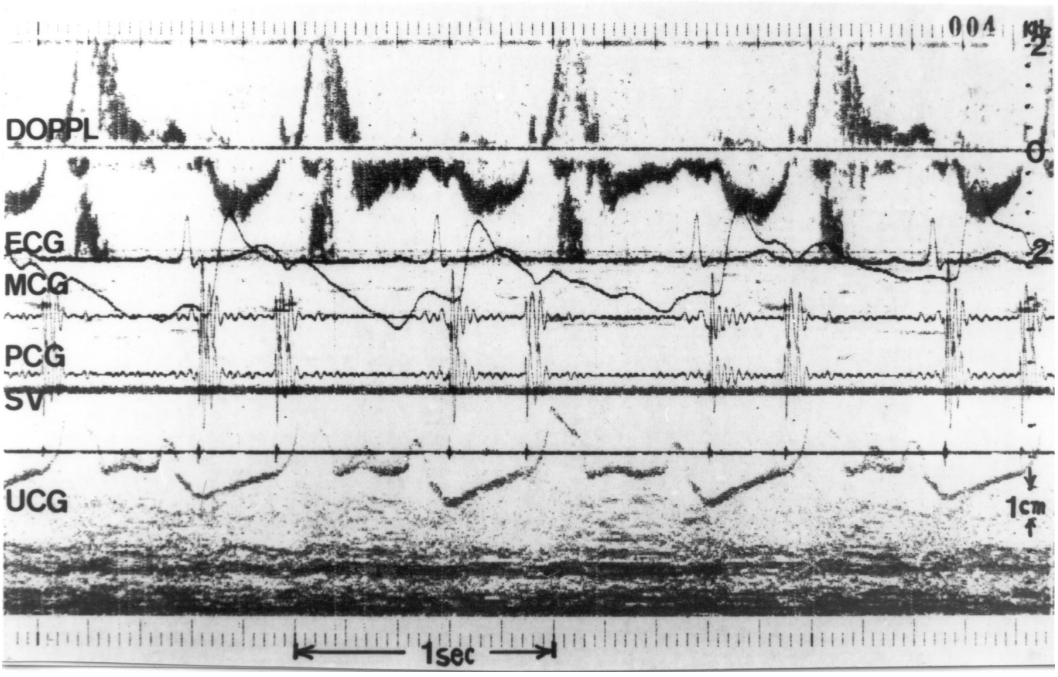

Fig. 9. An example of the record obtained by using the multi-recording system developed in 1970.

the cardiac chambers. It is considered that deformability is reflected on the flowing state of the intracavitary blood and on the pressure distributions in the heart chambers. Therefore, for practically assessing the pump function in much more detail, deformability of the heart should be measured clinically.

For this purpose, it is indispensable to measure and to estimate not only the size, shape, and displacement of the heart structures and their interrelationships during cardiac cycle or disease processes, but also the hydrodynamic information such as the flowing state (laminar or turbulent), the moving direction and flowing volume of the blood at the local portion in heart chambers, pressure differences between the local parts in the same chamber, and two- or three-dimensional pressure distribution in the cardiac chambers. At the initial stage, Tanaka et al. developed the biplane cardiotomographic method with high speed mechanical scanning in 1978 [61]. For visualizing the intraventricular blood flow, the contrast method in the two-dimensional echocardiography using the saline injection technique via cardiac catheterization was also done in 1978 [62].

However, it was considered that the ultrasonic Doppler method was adequate as a method for the collection of hydrodynamic data of intracardiac blood flow, because accurate velocity data could be obtained without disturbance of the blood flow process, as compared, for example, with the insertion of a transducer. Moreover, if an appropriate technique of velocity data processing were to be developed, the hydrodynamic data for clinical evaluation of the pump function could be deduced non-invasively.

Then, Tanaka, Ohtsuki (Tokyo Institute of Technology), and their colleagues began to develop the transthoracic technique for the ultrasonic Doppler method, which could be applied to detect flow velocity of the intracardiac blood.

1. Development of the Ultrasonic Doppler Method with Depth Resolution: In 1967, Okujima and Ohtsuki [63], [64] began development of a new ultrasonic Doppler flow meter system with depth resolution. At that time, many investigators used continuous wave ultrasonic Doppler methods for the detection of blood flow velocity in peripheral vessels [1], [3], [14], [66], [67].

At the beginning of this investigation, the ultrasonic pulsed Doppler equipment made in our laboratory could not be used for detection of intracardiac blood flow velocity because of insufficient gain in the amplifier and poor SNR [63], [64]. Development and clinical application of the "M-sequence modulated ultrasonic Doppler method" was accomplished at that time (1970), which made it possible for the blood flow velocity data in the heart chamber in living state to be obtained non-invasively, as illustrated in Fig. 11 [65].

In 1975, the multichannel Doppler system was developed [66], [67] in which real time analysis of the Doppler signals received was realized by introducing the heterodyne analyzing method. Moreover, the Doppler method and two-dimensional echocardiography were used in combination such that an arbitrary target space within the heart could be selected, with reference to the two-dimensional echocardiogram, and the blood flow velocity data at the target point and velocity profile along the beam direction for a distance of about 12 cm could be detected in real time. Fig. 12 shows an instantaneous velocity profile display of the intracardiac blood flow in the rapid filling phase in a normal subject. The thick arrows on the two-dimensional echocardiogram indicate the beam direction.

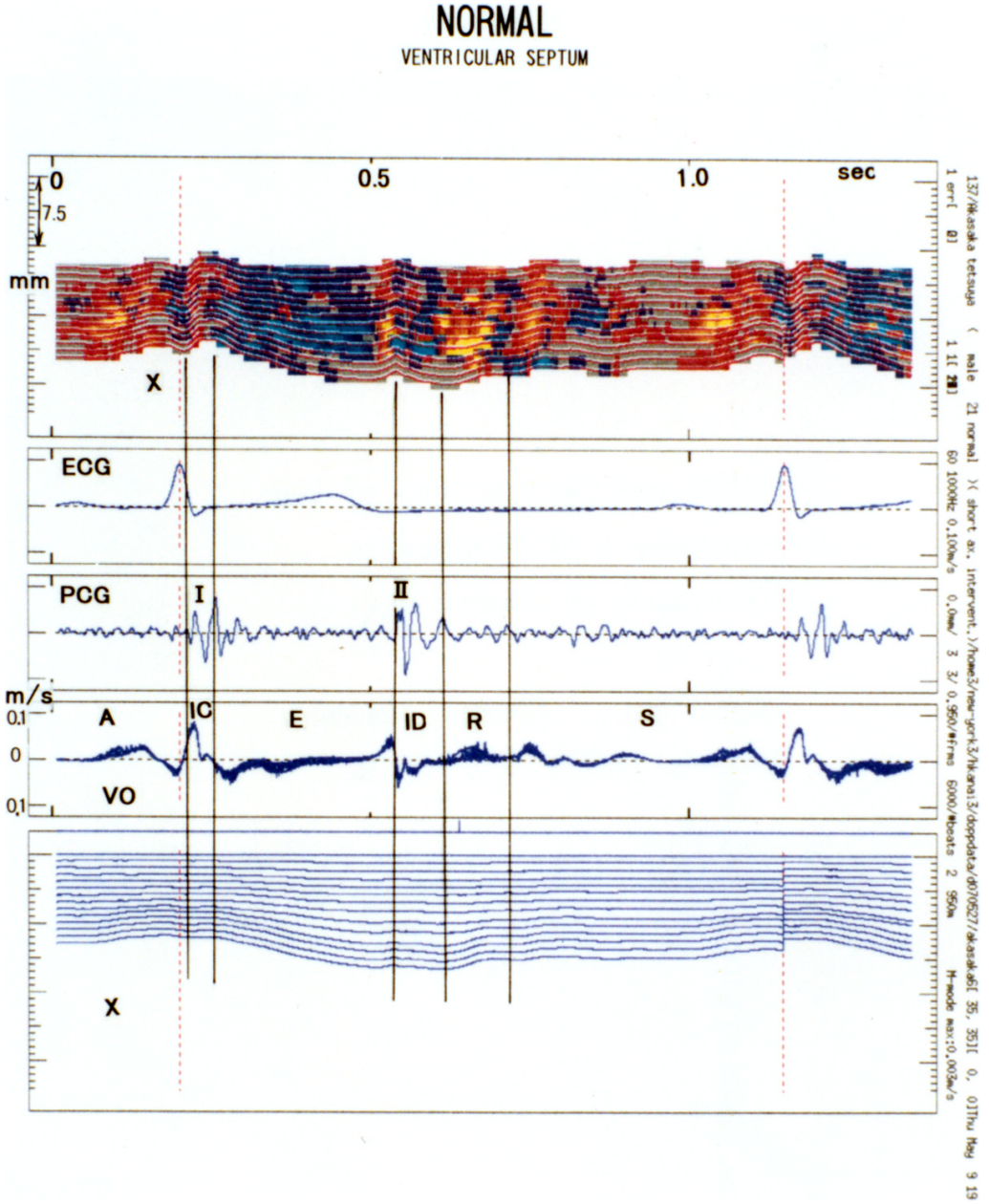

Fig. 10. Changes in thickness moving speed of the regional myocardium in the ventricular septum in a normal case measured by the phase difference tracking method. The distance between two adjacent points is about 0.75 mm. Color distribution shows the normalized speed of change in thickness. Blue indicates +5 m^2/s, and yellow indicates −5 m^2/s. Upper panel: Superimposed display with M-mode and thickness change and normalized speed change in thickness. Lower panel: Thickness change. Middle panel: Overlapped display of the speed of whole points. A = Atrial contraction, IC = isometric contraction, E = ejection, ID = isometric dilatation, R = rapid filling, and S = slow filling.

Then, if the flow velocity profile along the beam axis was obtained by changing the beam direction on the scanning plane at the same cardiac phase, the two-dimensional velocity distribution at an arbitrary cardiac phase could be obtained by special interpolation between two adjacent velocity profiles and displayed as a color coded pattern [72].

In 1980, a new ultrasonic pulsed Doppler technology was developed that could measure the flow velocity at an arbitrary portion of the heart chamber [70], [71]. Doppler signals recorded at multiple sampling points on the apical long-axis section plane are analyzed with the FFT method in real time [73].

2. Development of the Data Processing Technique for Detecting Hydrodynamic Information from Doppler Velocity Data: The important parameters for hydrodynamic information for estimating the pump function are flow volume, pressure, and their changes during the cardiac cycle. Furthermore, from the clinical point of view, it is the most convenient for an intuitive evaluation of cardiac function, provided that the hydrodynamic information is represented as a two-dimensional distribution image on the ultrasonic scanning plane.

Since 1982, Tanaka et al. have been developing the following two new data processing techniques based on hydro-

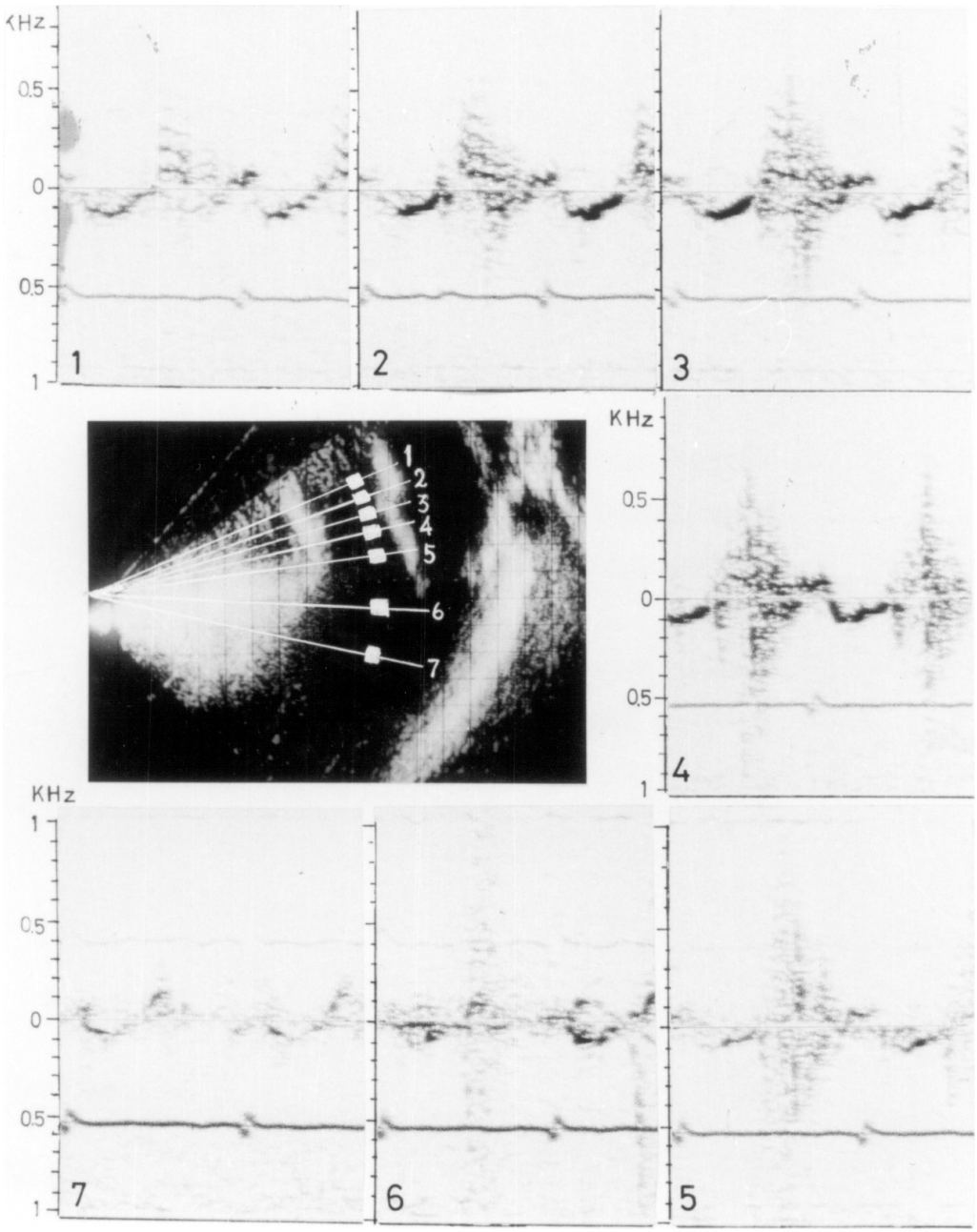

Fig. 11. Intraventricular blood flow velocity pattern obtained from a case of aortic insufficiency by the M-sequence modulated ultrasonic Doppler method combined with the ultrasono-cardiotomography in 1970. Flow velocity data were detected at the white areas ($1 \sim 7$) indicated on the tomographic image and analyzed with a sonagraph. In the diastolic phase, regurgitant velocity patterns with high frequency harmonics are represented.

dynamics, i.e., two-dimensional distribution of blood flow volume on the ultrasonic scanning plane [74]–[77] and two-dimensional distribution of dynamic pressure and pressure differences on the scanning plane [78], [79].

3. Two Dimensional Distribution of Blood Flow Volume on the Scanning Plane: For this purpose, displaying the stream line distribution is most appropriate for intuitive understanding of local and whole blood flow volume and flow state in the heart chamber on one scanning plane. This is because the stream line represents the direction of the velocity vector of the flow and the interval between two adjacent stream lines represents the flow volume [80]–[82].

The velocity data obtained at a point on the ultrasonic beam by the ultrasonic Doppler flow meter system with depth resolution are divided into two components, namely the Uz component in the X-Z plane and the Uy component in the X-Y plane. The Uz component is concerned with intersecting flow, and the Uy component is concerned with flow parallel to the scanning plane. Accordingly, the two-dimensional distribution of the Doppler velocity on the ultrasonic scanning plane is also contained on the two velocity components, because the blood flow in the heart chambers is spatially three-dimensional. To obtain the stream line distribution on the scanning plane, it is necessary to

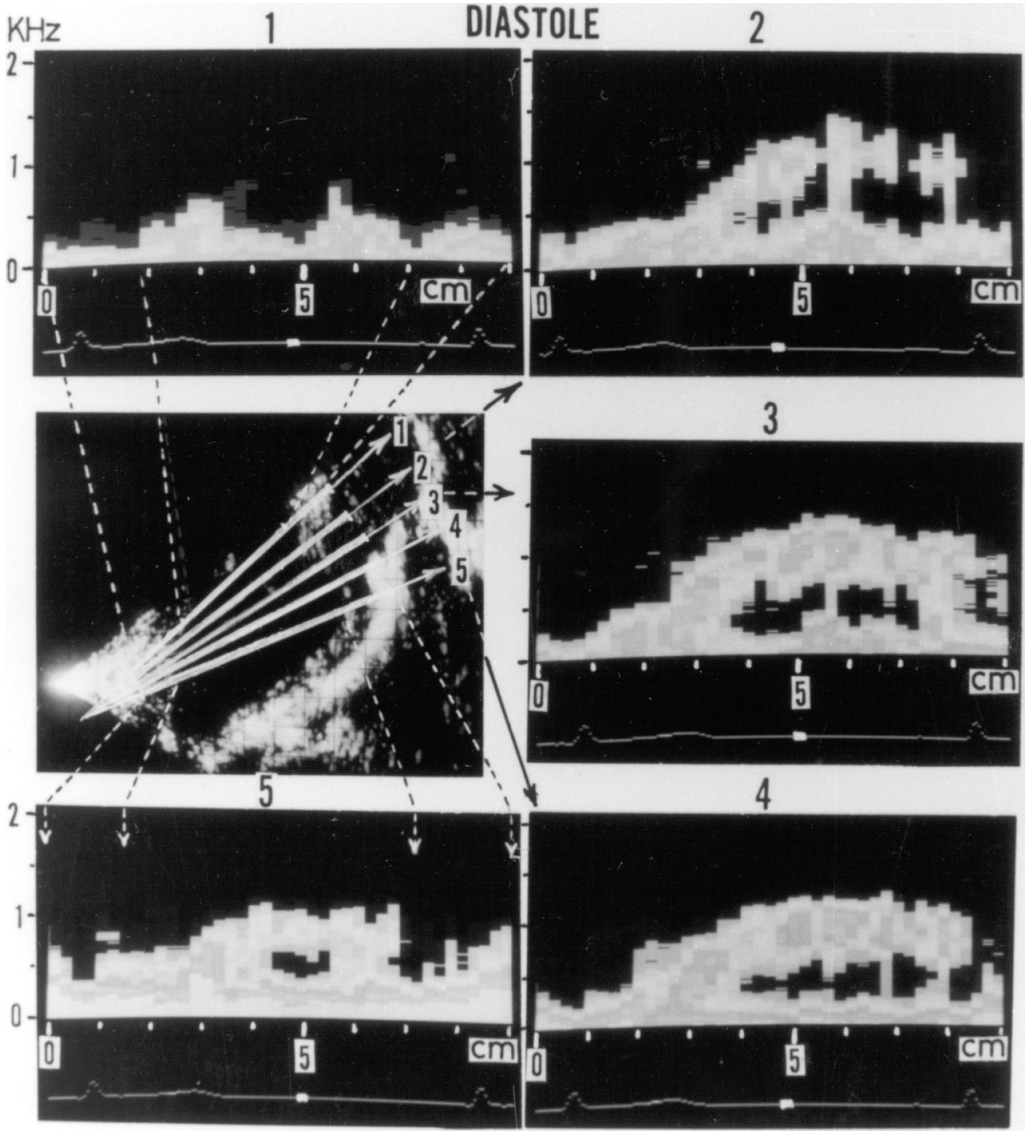

Fig. 12. Instantaneous velocity profiles of the intracardiac blood flow during diastole (phase shown by a white dot on the ECG), which were obtained in the left ventricle in a normal case in the various beam directions ($1 \sim 5$). Beam directions were confirmed by the ultrasonocardiotomogram that was simultaneously recorded.

give consideration to these two flow components. Ohtsuki and Tanaka developed a new concept on the flow function theory in 1997 [83], which established the method for obtaining the stream line distribution on an arbitrary section plane in three-dimensional flow, allowing the characteristics of the flow to be visualized and evaluated.

The flow function $[Q(X,Y)]$ consists of two kinds of functions. One is the boundary function $[Q_b(X,Y)]$, which is considered to exist at the source of inflow (Si) and outflow (So) and is positioned at the boundary of the observing plane (scanning plane); the flow appears parallel to the plane and is called two-dimensional flow. The boundary function is the same as the stream function in two-dimensional flow. The other is the fundamental flow function or the laminary flow function $[Q_p(X,Y)]$, which is considered to be at the Si or the So from the scanning plane and is at the point source dispersed on the observing plane with the flow appearing perpendicular to the plane. The Si represents a positive source and is shown on the observing plane as a green-colored point. The So represents a negative source, or a sink, and is shown as a pink-colored point. The flow function $[Q(X,Y)]$ is represented as $Q\,(X,Y) = Q_b(X,Y) + Q_p(X,Y)$.

Accordingly, from the data thus obtained by both calculation of the boundary function and the fundamental flow function, the flow function is calculated, and equiflow function lines are drawn at each interval of the unit flow volume, corresponding to the quantized step, yielding the stream line distribution, which begins at the positive source and ends at the negative source.

Fig. 13 shows the two-dimensional distribution of the stream lines in systole obtained from a normally functioning case (upper pictures) and an infarction case (lower pictures). The pictures on the left were taken during the

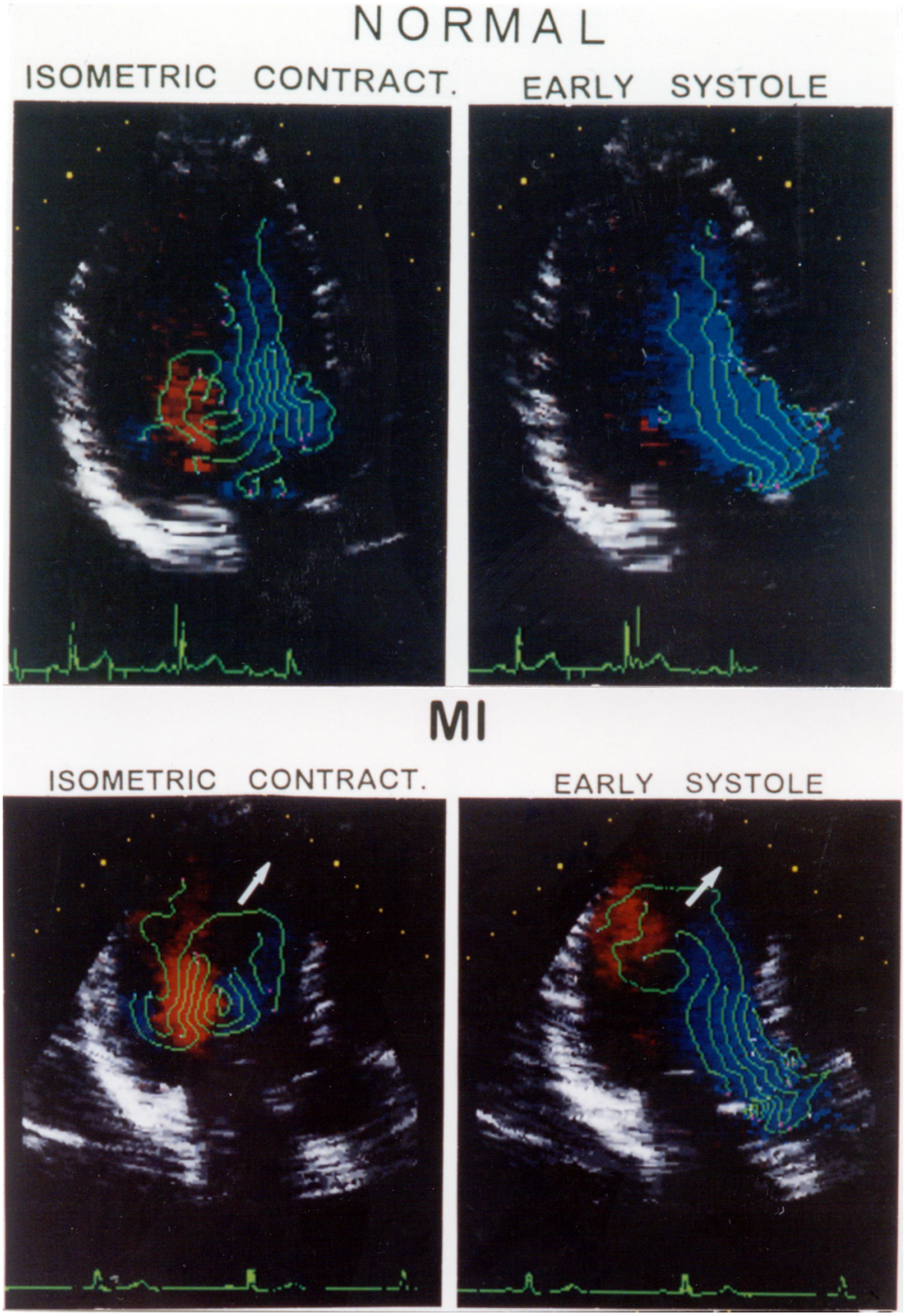

Fig. 13. 2-dimensional distribution images of the stream lines in normal (upper panel) and myocardial infarction (lower panel). Stream line begins at the positive source (green-colored dot) and ends at the negative source (pink-colored dot). Flow state and local flow volume were quite different between normal and infarction.

isometric contraction (IC) phase, and the picture on the right was taken during the early systolic phase. The stream lines in the outflow area show a relatively smooth pattern, although the circular pattern is observed at the postero-basal area of the ventricle in IC. The figures show a circular or a semicircular pattern of the stream lines at the apical area of the left ventricle during systole. The case of antero-septal myocardial infarction, a ventricular aneurysm (white arrow), is clearly visible in the apical area. These findings show that the circular pattern of the stream line indicates rotating flow and that, in the ventricular aneurysm, abnormal rotating flow appears at the beginning phase of systole. From the stream line distribution thus obtained, flow direction, flow volume at the local area, and the characteristics of three-dimensional flow can be evaluated visually and quantitatively.

The interval between two adjacent stream lines indicates flow volume in cm^2/s. Thus, one-dimensional flow volume distributions along the line normal to the stream line indicate a representative flow passing through the short axis cross-section plane and the integrated value of the area of this distribution represents the instantaneous flow volume passing through the short axis cross-section of the ventricle during a particular cardiac phase (Fig. 14).

Provided that the instantaneous flow volume, mentioned previously, is recorded continuously during one cardiac cycle, the flow volume, which is equivalent to the stroke volume or cardiac output, and the flow volume curve during one cardiac cycle are obtained as shown in Fig. 15.

When the difference in flow volume between two time points is obtained, that difference indicates the work in displacing the blood from the ventricle, the portion below the selected short axis-cross section plane, as shown in Fig. 14. When a difference in flow volume is obtained between two different cross-sectional planes at the same time, that difference determines the deformability of the limited portion of the ventricle existing between the two cross-sectional planes, as shown by the differences between two adjacent flow volume curves in Fig. 15.

As understood from these results, much useful information regarding pump function became known as pump function index, for example, cardiac output, stroke volume at various portions of the ventricle, work, flow rate, ejection rate, ejection loss, energy loss, etc., as well as information regarding the flow state, acceleration rate, and hydrodynamic data [84]–[86].

VI. Two-Dimensional Distribution of Dynamic Pressure and Pressure Difference in the Scanning Plane

When a pressure difference appears in a fluid, the fluid moves from the high pressure region to the low pressure region, and flow occurs. Thus, a close correlation exists between the velocity of flow and the pressure difference, as understood from Euler's equation of motion.

In 1983, Tanaka et al. pointed out the following correlation from the results obtained [87], [88] from physical experiments using the narrowing flow model, viz., maximum velocity $\fallingdotseq$ 41.3× (pressure difference)$^{0.57}$. These facts strongly suggested that details of the two-dimensional distribution of pressure and pressure differences, which are indispensable for producing the flow in the chamber, can be obtained from two-dimensional velocity distribution data (B-mode Doppler velocity), if the processing technique is adequate for deducing the pressure values from the velocity distribution data.

Since then, in 1986, Tanaka et al. developed a new processing method for visualizing the two-dimensional pressure (dynamic pressure) distribution on the scanning plane and the one-dimensional pressure distribution along the line set on the cross-sectional view of the heart [78], [79].

By using the two-dimensional distribution of the velocity component (u) measured by the pulse Doppler method, the velocity component (v) orthogonal to the beam direction is deduced by applying the flow function theory [78], [81], [82]. Thus, the B-mode Doppler acceleration (A_{db}), which is calculated by using the velocity components of the two-dimensional velocity distribution on the scanning plane, can be obtained based on the Euler's equation of motion:

$$\frac{D\vec{v}}{Dt} = A_{db}$$

$$-\nabla p = \rho \cdot A_{db}$$

where $\vec{v}$ is the deduced average velocity vector on the scanning plane, ρ is density of the medium, and p is pressure. From linear integration performed along the line connecting the reference point to the observation point on the plane, i,e.,

$$p = -\rho \int_1 A_{db \times d1}$$

the Doppler pressure and the velocity on the scanning plane can be deduced from the Euler's equation of motion as

$$P\,d = \mathrm{P\,r}\,ef + \rho \int_l \left(\frac{\partial \vec{v}}{\partial t} + (\vec{v} \times \bigtriangledown \vec{v}) \right) ds$$

where l is length of the path, ds is unit area in the scanning plane, and $\mathrm{P_{ref}}$ is the pressure at the reference point on the plane. Although P_d thus calculated is a multi-valued function that depends on the path, the equi-pressure lines can be obtained in the same manner as that in the flow function. Thus, the Doppler pressure distribution on the scanning plane can be decided from the two-dimensional velocity distribution data on the scanning plane set in the moving fluid in three dimensions [89]–[92].

In practice, the two-dimensional distribution of the equi-pressure lines overlaps the B-mode echo image, and quantitative pressure distributions along the line, which is set arbitrarily on the B-mode image, are used.

The Doppler pressure thus obtained is different from the pressure measured by cardiac catheterization, which

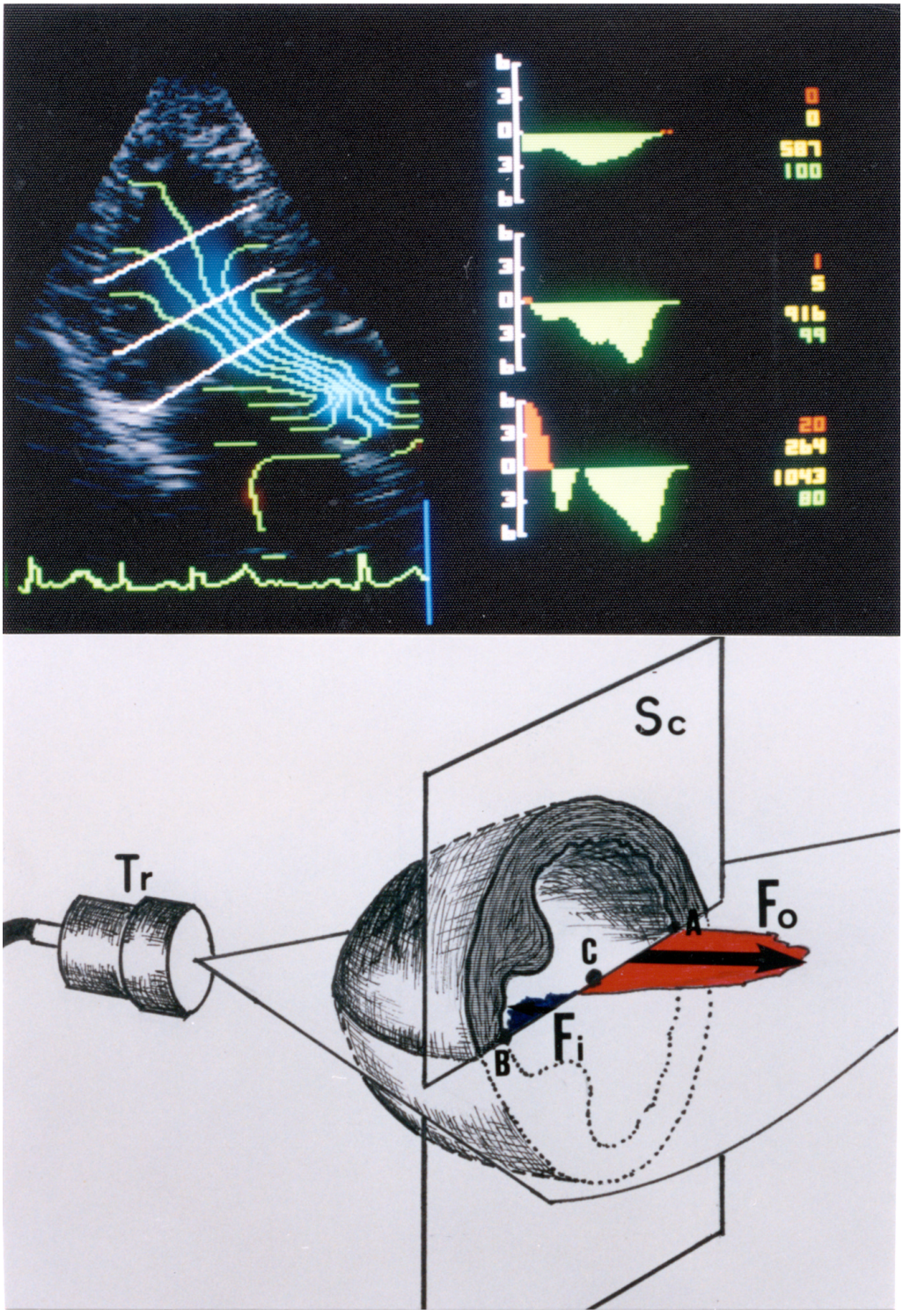

Fig. 14. Right-side patterns in the upper picture show the 1-dimensional flow volume distribution at a particular systolic phase along the arbitrary three lines drawn on the 2-dimensional stream line distribution (left side). The 1-dimensional flow volume thus obtained indicates the representative flow volume passing through the short axis plane such as F_o and F_i in the lower schemetic picture. The A-B line on the S_c corresponds with the white line on the 2-dimensional echogram.

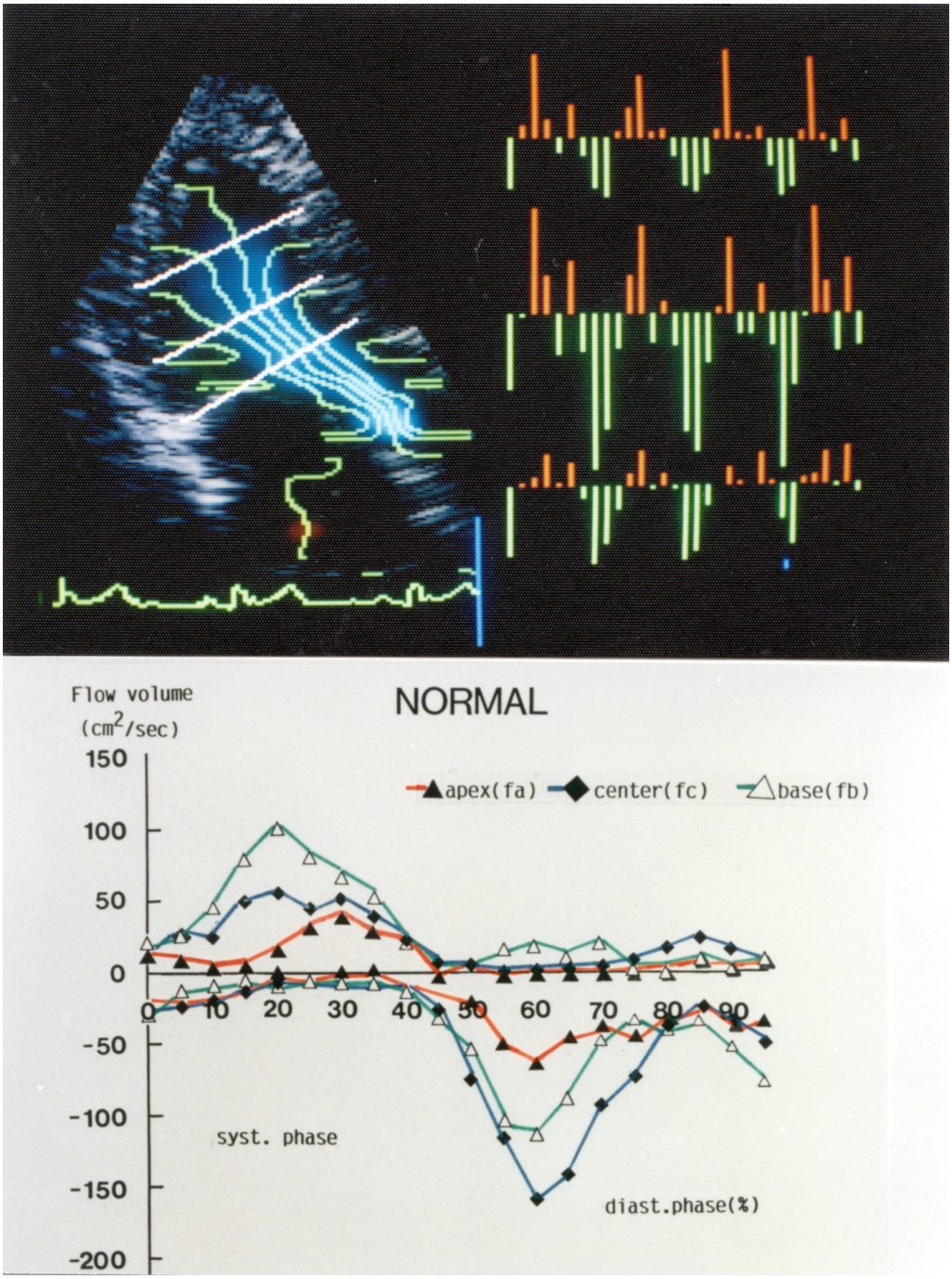

Fig. 15. Flow volume change at three positions [1 to 3 portion; apex (f_a), center (f_c), and base (f_b) on the tomogram] in the left ventricle during one cardiac cycle. The length of the bar graphs shows the flow volumes at the particular cardiac phases. Right upper bar graphs indicate the changes in the flow volume at the various cardiac phases during three cardiac cycles. The three lines of the bar graph were obtained along every three white lines on the tomogram. Lower curves show the flow volume curves obtained from the envelope of the bar graph at the three portions.

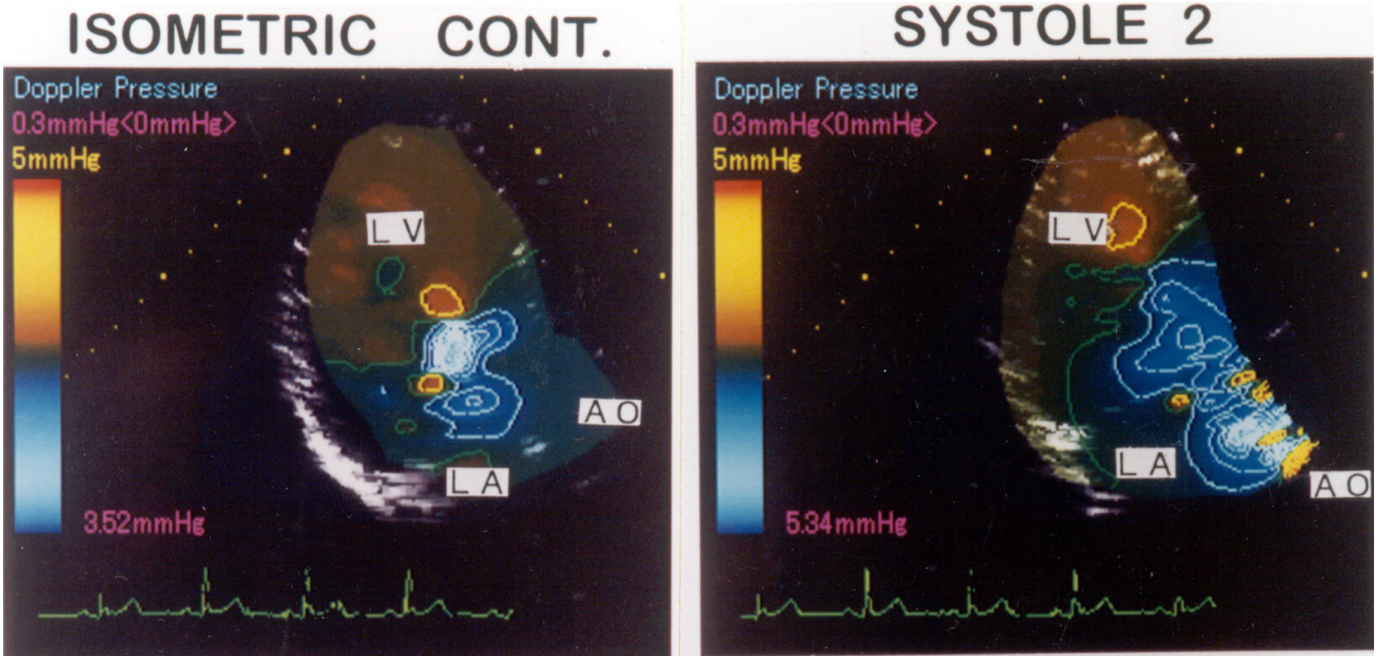

Fig. 16. 2-dimensional Doppler pressure distributions at two cardiac phases in systole obtained from a normal subject. The pressure value is represented by equipressure lines. Intervals between two adjacent pressure lines are 0.3-mm Hg step. The maximum pressure difference in each cardiac phase is shown at the left lower corner by the number. The red-colored area shows relatively higher pressure area, and the blue-colored area shows the lower pressure area. The green line indicates the standard level (0 level).

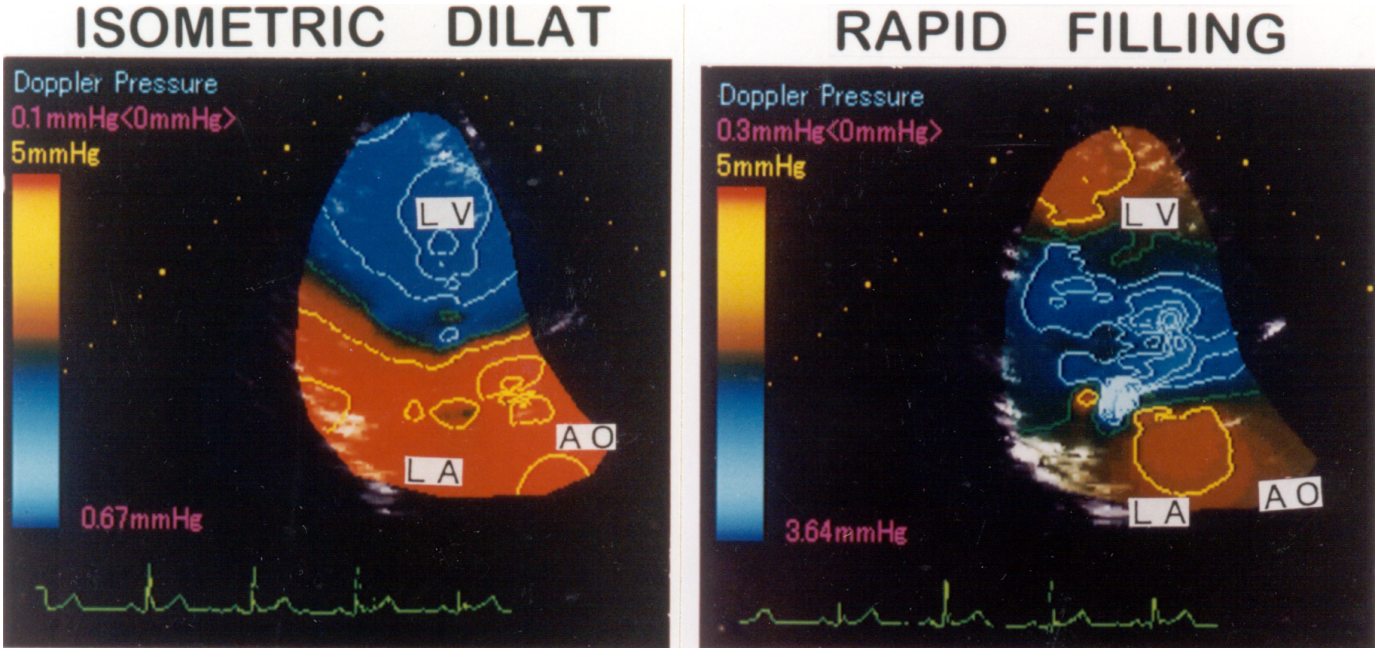

Fig. 17. 2-dimensional Doppler pressure distributions at two cardiac phases in diastole in a normal case.

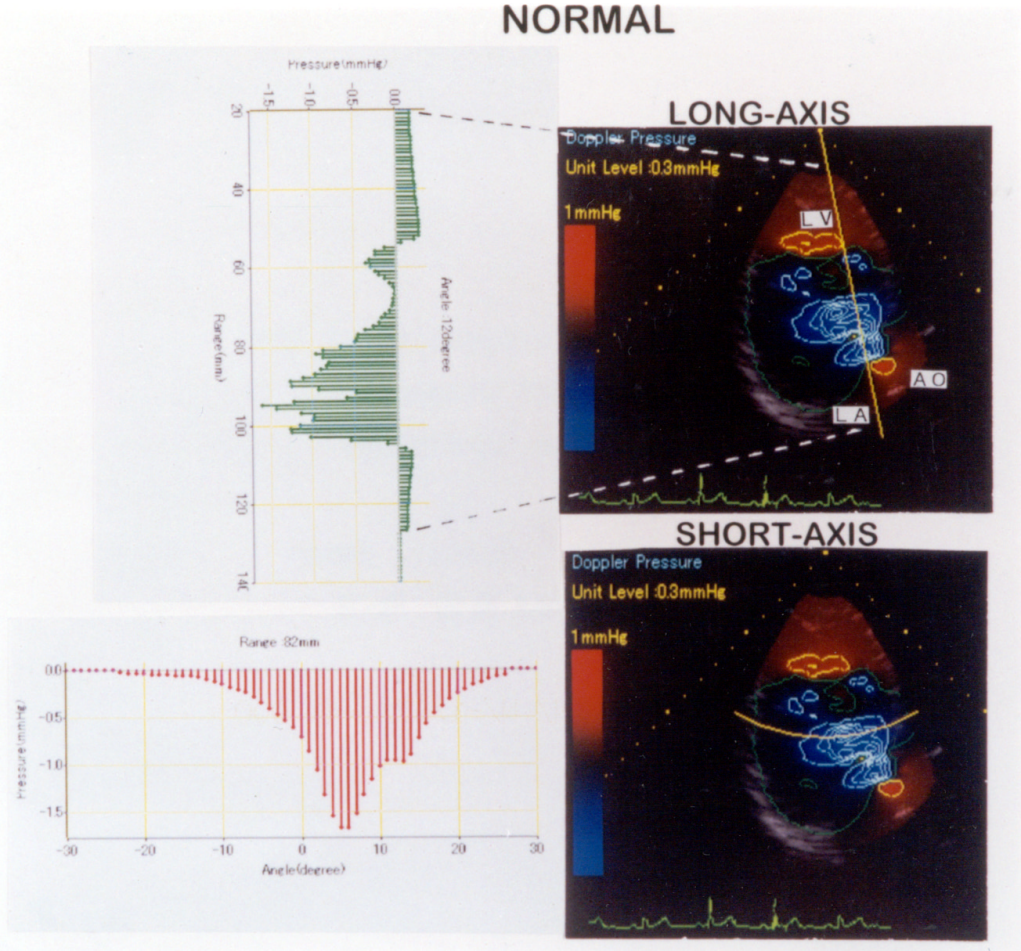

Fig. 18. 1-dimensional pressure distributions along the line of the outflow tract (upper left) and along the line of the short axis of the ventricle (lower left) at the ejection phase in a normal case.

is total pressure, and is nearly the same as the dynamic pressure, viz, the pressure required for the displacement of the blood from one point to another. Accordingly, it reflects the manner in which the force generated by contraction and extension of the regional myocardium acts on the blood, and it can be said that the changes in the Doppler pressure pattern during the cardiac cycle represent the deformability function of the ventricle.

Fig. 16 is an example of the two-dimensional Doppler pressure distribution during the IC and in late systole for a normal case, and Fig. 17 is that for isometric dilatation and rapid filling phases. Fig. 18 shows the one-dimensional pressure distribution along the outflow tract (left upper picture) and that along the short axis of the ventricle (left lower picture) during systole for a normal heart. From these facts, it can be said that changes of the pressure distribution pattern during pulsation clearly indicate the deformability of the ventricle.

There are still many problems that must be solved, e.g., the hydrodynamics of blood flow in the heart chambers. However, it is expected that the methods mentioned previously will become indispensable for accurate, timely clinical cardiology diagnostics.

VII. Conclusion

In this paper, the progression of the developments of the ultrasonic application for visualizing and measuring the structure and function of the heart in our laboratory since 1960 has been described. Our projects surrounding ultrasonic application in cardiology were performed systematically in close collaboration with engineering and medical groups and also with Japanese and USA staffs internationally for about 40 yrs. The author would like to thank especially F. Dunn, (University of Illinois) for close collaboration and instruction. At this time, it can be said that the application of ultrasound to cardiology is certainly progressing. Until now, ultrasound has been chiefly applied to evaluate and measure the mechanical events in cardiology. However, there still remain many other functions in the cardiovascular field to be evaluated visually other than the mechanical events, e.g., biochemical events, a new frontier to be studied.

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