Short History of The Development of Echocardiography With Special Reference to That in Japan (1)*

Yasuharu Nimura, MD, MSc, FJCC**

Abstract
The ultrasound reflection technique was introduced into cardiology in 1953, and in 1955, the ultrasonic Doppler technique was introduced. The dawning stage of ultrasound diagnostics of the heart was the ten year period prior to 1965. During this stage, besides the afore mentioned techniques, there were only a few attempts to use ultrasound for heart diagnostics.

In the next age, from about 1965 to 1975, the leading type of the cardiac ultrasound was M-mode echocardiography. M-mode echocardiography was the first generation of ultrasound diagnostics of the heart used in routine practice. This period may be called the age of M-mode echocardiography. During 1975 to 1985, the leading technique was real-time two-dimensional echocardiography, with and without the Doppler mechanism, which was the second generation in routine. This period can be called the age of the two-dimensional echocardiography. The period from 1985 to the present time may be called the age of the color Doppler, which has been the third generation of the cardiac ultrasound. However, since the middle of this last age the cardiac ultrasound has been showing the most diversification of techniques and usages. Therefore, it is uncertain whether the age division as mentioned above can be continued. The period extending over the last age and present time may be the second dawn of the cardiac ultrasound.

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sense. Therefore, studies on cardiac ultrasound started a little after the other organs because of heart motion, and had taken different courses.

I. Introduction of the Ultrasonic Reflection Technique into Cardiac Diagnostics

The first work of the cardiac ultrasound was done by W. D. Keidel [1]. He attempted to measure the heart volume on the basis of ultrasound absorption by the heart, transmitting 60KHz ultrasound through the thorax. However, he could not obtain good results. Therefore, the gate to ultrasound diagnostics of the heart was really opened by I. Edler and C. Hertz.

I. Edler, a cardiologist, was specialized in cardiac catheterization in Lund, Sweden (Fig. 1). He consulted with C. Hertz, a physicist, in 1953, about whether there were any diagnostic tools which did not give physical load and pain like those by catheterization, to any examinee. Hertz advised Edler to use ultrasound [2]. They began their study in May of 1953. They could obtain echoes that were assumed to be originated from the heart, using the A-mode method. However, the A-mode images were difficult to distinguish between each echo source of the echoes displayed. Edler and Hertz set an M-mode monitor to make a motion pattern of each echo as reference for distinguishing echo sources on the A-mode image. Consequently, however, the M-mode image began to play the leading role with the progression of their study [3].

The M-mode image usually showed an echo demonstrating a motion with a rectangular pattern through the transthoracic approach near the left sternal edge at the third intercostal space in cases of mitral stenosis [3] (Fig. 2). Then, it was found that the normal pattern of that echo showed two peaks in one cardiac cycle [4]. The source of that echo was considered to be the anterior wall of the left atrium, being based on anatomy and physiology [4].

In those days, the diagnostic value of the above rectangular pattern for mitral stenosis attracted attention in cardiology. In the late 1950s, already, Effert [5], Gassler [6], Grossse-Brockhoff [7], Schmitt and Braun [8] reported on the rectangular echo in mitral stenosis, respectively. In addition echocardiographic features of the left ventricular posterior wall, the left atrial myxoma, and pericardial effusion were also known.

After that, with the progress of the study of echocardiography, a doubt had arisen concerning the echo source of “the echo of the anterior wall of the left atrium.” In those days, Nimura, Satomura, Yoshida, and their coworkers had already reported on the mitral...
valve Doppler signal (See Chapter II). The concerned echo source was reexamined by Edler [9-11]. Consequently, "the echo of the anterior wall of the left atrium" was corrected as "the echo of the anterior leaflet of the mitral valve[10]."

As generally known, the anterior mitral valve echo has been an important landmark for the echocardiographic examination up to the present time. Because this echo was confirmed, the first step of echocardiography is considered to be established as heart diagnostics (See footnote 1).

First of all, it is especially significant that the intracardiac structures have come to be observed in its natural condition in situ.

In the early 1960s, besides the above mentioned laboratories in Europe, echocardiography had begun to be studied by Joyner and coworkers [13,14], Feigenbaum and coworkers [15], and so forth in the United States, Chih-Chang Hsü (徐智章) [16] in China, Nagayama and his coworkers [17], Nimura and his coworkers [18], and Tsunemoto and his coworkers [19] in Japan. However, echocardiography was never widely known. In short, the late 1950s and early 1960s marked the dawn of echocardiography.

II. Dawn of the Ultrasonic Doppler Diagnostics in the Cardiovascular Field

S. Satomura, a physicist, and Y. Nimura, a cardiologist, started their study to introduce the ultrasonic Doppler technique into the cardiovascular field in 1955. Since around 1952, Satomura had been devising a new technology to measure velocity of a target on the basis of the ultrasonic Doppler effect, by analogy with radar technology. Satomura aimed to use the Doppler technique for the physical measurement in science and industry. However, his superior, Prof. Kinjiro Okabe, advised him to try a medical use of the Doppler technique. Heart motion was considered to be a suitable target. However, because Satomura was a layman in medicine and had no knowledge on anatomy and physiology of the heart, he appealed to medical circles to study the Doppler technique from the medical aspect. Thus, the above mentioned interdisciplinary study [20-23] was formed between Satomura and Nimura with his coworkers.

The general feature of the cardiac Doppler signal was apparently an irregular group of waves of about 100Hz in correspondence to one cardiac cycle (Ultrasound beam of 3MHz was used) (Fig. 3). It shows a variety of features, depending upon changes of the site of the transducer and those of the beam direction. The aim of the study was to demonstrate whether any useful diagnostic information was obtained from the above Doppler signal.

The Doppler signal was considered to be caused by
movements of cardiac structures, mainly of the heart wall, and apparently did not seem useful. However, after two years Nimura and his coworkers succeeded to separate high-pitched snappy Doppler signals, considered to be caused by the opening and closing of the heart valve, from the raw signal by data processing with filters, amplifiers and so forth (Fig. 4)[23-27]. In those days, while echocardiography had been clinically used in Europe, the valve echo had not yet been established. Reaching the concept of information of the intracardiac structure was earlier in the cardiac Doppler than in the cardiac echo.

The ultrasonic Doppler technique enabled one to noninvasively detect temporal relations and velocity of the valve movement first. The prolongation of isometric relaxation is an early manifestation of left ventricular diastolic failure. It was already demonstrated with the valve Doppler (Fig. 5) [28].

In short, the results obtained above were considered to reveal that the ultrasonic Doppler technique had capability for Doppler diagnostics.

In the Doppler signal of the heart, it was considered that the low-pitched component of about 100Hz was originated from the heart wall, holding the greater part of the Doppler output energy. In those days, this component had not seemed to be analyzed easily, and then had been left as unavailing up to the 1990s, when the tissue Doppler imaging appeared. The low-pitched component corresponds to the tissue Doppler imaging of the ventricular wall and ventricular septum, although the technological approaches are somewhat different between the former Doppler and the tissue Doppler imaging. (See Chapter IX)

By the way, the raw cardiac Doppler had included weak and lasting noisy signals besides the low-pitched signal of about 100Hz and the high-pitched snappy signal, i.e., valve signal. Similar signals to the weak noisy signals had been also detected on the thoracic aorta. They had been considered to be related to small vibrations of the heart wall or intracardiac blood flow. However, further analysis had been impossible, because of lack of sufficient gain of the equipment used. In that time, Ziro Kaneko, a psychiatrist, asked Satomura for some collaboration to study brain circulation. Their collaborative study was started in January, 1958. In the process of collaboration, they tried to apply the Doppler technique to the carotid artery, but not to the intracranial vessel, because the ultrasound beam could hardly pass through the skull. Kaneko and Satomura
could detect the noisy signal clearly from the carotid artery. It exhibited pulsatile rhythm and showed variations of wave patterns in response to those of the underlying conditions of the examinee (Fig. 6). Being based upon the above-mentioned features, the noisy signal was considered to be caused by the blood flow. Thus, the concept of blood flow Doppler signal came into existence[30-32]. Kaneko named their equipment “Blood rheograph.”

Here, it should be noted that there are some disturbances in information on the early stage of the Doppler technique in medicine. What is described here is the truth (See Footnote 2).

In 1961, D.L. Franklin, R.F. Rushmer, and their coworkers also reported Doppler flowmetry [33]. It was noteworthy that their system was already applied on animal experiments by wireless in a few years [34]. However, their system does not seem to be used widely later.

In 1962, Kanemasa Kato experimentally demonstrated, in cooperation with Kanako and his coworkers, that the blood flow Doppler was originated mainly by Rayleigh scattering of ultrasound from blood corpuscles [35]. Power of the Doppler output was proportional to the number of corpuscles per unit volume in fluid. This relation will be the basis of quantification of Doppler flowmetry.

The original type of the Doppler technique could not detect flow direction. In 1966, Kato and his coworkers devised a new Doppler technique that could detect flow direction [36]. In the same year F.D. McLeod also devised a directional type of Doppler technique based on a different principle from that of Kato [37]. The progress of the directional Doppler technique enabled one first to know that there was often a

Footnote 2: The source of the disturbances has been Satomura’s exceptional paper, i.e., reference 29. This paper caused misunderstanding in Japan and abroad, as if he were the discoverer of the valve signal. This paper was not Satomura’s own achievement, but an early leakage of the references 22-27 without permission. Although Satomura was one of the members of the interdisciplinary study group, he was a layman in medicine and had no direct contribution to establish the valve signal. It seems the reason for Satomura’s carelessness that he was a physicist and did not know so much about general rules for writing original papers in medicine. He also admitted his carelessness, but it was too late to withdraw or correct the paper. The valve signal was identified directly by Nimura and his medical coworkers. Of course, Satomura was one of the non-medical coworkers. According to Kaneko’s personal communication, Satomura committed similar mistakes also concerning the flow Doppler in the collaborative work with Dr. Kaneko.

Fig. 6.
Variety of Doppler flow patterns of the common carotid artery, recorded with an electromagnetic oscillograph. The frequency spectrogram had not yet been used for displaying the Doppler signal.
(By Kaneko et al., 1958)

Fig. 7.
Directional Doppler technique. Upper: Flow pattern of the femoral artery recorded by the directional Doppler technique. Flow toward and away from the transducer are displayed under and over the base line, respectively.
Lower: Flow pattern of the femoral artery recorded by the non-directional technique. In this case flow is displayed over the base line. The directional Doppler technique demonstrates that the femoral arterial flow has a reverse flow phase in a pulse period, following the early rapid phase.
(By Kato et al., 1966)
reverse flow phase in the Doppler velocity wave in a vessel and that a forward flow and a reverse one often simultaneously coexist in a cross-section of a vessel during the turning phase between the forward and reverse phases (Fig. 7).

III. Contributions of Japanese Researchers to the Cardiac Ultrasound in the Early 1960s

1) Correspondence between the echo and the Doppler

As described above, the mitral echo and the mitral Doppler were first obtained separately in different laboratories, respectively. Then, it seemed to be necessary to confirm that the mitral echo and the mitral Doppler were caused by the same target. For this purpose, Kato, Nimura, and coworkers devised an equipment as follows [38]: a circular transducer consisting of a central disc and an outer layer, one for the Doppler and the other for the echo; the ultrasound beams were coaxial, but had different frequencies for the Doppler and for the echo; this equipment enabled one to simultaneously operate the Doppler and the echo toward the same direction [38].

The study was performed on healthy subjects, using the mitral Doppler as a landmark. The echo that was simultaneously obtained exhibited a two-peaked pattern in correspondence to one cardiac cycle. The Doppler and the echo showed a good correspondence in the time of occurrence and velocity of rapid movements [39]. So, the Doppler and the echo obtained were considered to be originated by the same target (Fig. 8). The echo pattern obtained here was also very similar to that obtained in Edler’s laboratory. Thus, it was confirmed that the mitral Doppler obtained in Japan and the mitral echo obtained in Europe were obviously originated by the same target. Similar results were obtained in cases of mitral stenosis to that in healthy subjects. Good correspondence between the echo and the Doppler was considered to generally support reliability of the ultrasound examination.

2) Ultrasonic intravenous sonde

Studies on two-dimensional echocardiography had begun on a different line from that of M-mode echocardiography. In the late 1950s, two-dimensional echography had been more or less used for diagnosis of diseases in parenchymal organs, e.g., diagnosis of breast cancer, that of intracranial tumor, and so forth, but not for heart diseases. In order to apply two-dimensional echography for the heart in those times, it was necessary in advance to overcome the influence of the heart motion on the image quality. For this purpose, J.J. Wild [40], S. Olofsson [41], and A. Asberg [42] challenged this problem with their own unique scanners, respectively. But their attempts did not seem to be fruitful.

In Japan, R. Omoto and his coworkers [43,44], M. Tanaka, Y. Kikuchi, and their coworkers [45,46] and K. Sadamoto [47] studied on the transesophageal approach in the early 1960s. Their efforts also were not successful. The reason was that the mechanical structures of the probe did not fit the intra-esophageal scanning. After all, the transesophageal approach had not been developed up until the time when Frazin and his coworkers, Matsuzaki and his coworkers, Hisanaga and his coworkers, and Hanrath and his coworkers studied it with new types of a special probe, respectively, in the late 1970s, as mentioned later (See Chapter IX).
In 1962, R. Omoto and his coworkers succeeded to obtain a C-mode image of the atrial septal defect in humans with an ultrasonic intravenous sonde [43,48]. A transducer was mounted near the tip of a sonde, being directed perpendicularly to it. The sonde was inserted into the inferior caval vein from the femoral vein to put the transducer at the atrial level. The C-mode image was obtained by the combination of radial scan and longitudinal shift of the transducer in the right atrium. However, this type of the intravenous sonde did not develop to be used widely in the clinical setting.

In addition, concerning the ultrasonic intravenous probe, C. Cieszinski had also reported its usefulness in the previous year [49,50].

3) Ultrasono-cardio-tomography — An early type of two dimensional echocardiography, by Tanaka and Kikuchi, being synchronized with the electrocardiogram

A study of two-dimensional echocardiography was also begun by M. Tanaka, Y. Kikuchi, T. Ebina and their coworkers, on a different line from that of the M-mode one, in the early 1960s [51]. They started from basic studies of human tissue; they adopted some new ideas. The representative one of them was beam control mechanism in synchronization with the electrocar-
diagram to avoid the influence of heart beats. A water-immersed transducer was sited very closely to the body surface in the left intercostal space, being operated in sector scan, to avoid blocking the ultrasound beam by the ribs. They called their new technique ultrasono-cardio-tomography (Fig. 10).

Tanaka and his coworkers have particularly analyzed motion and morphology change of the heart with their own equipment for over ten years [52-54]. Nimura and his coworkers [55,56] in Japan and King [57,58] in the United States also studied two-dimensional echocardiography in synchronization with the electrocardiogram (Fig. 11). The control mode with the electrocardiogram was called the stop-action principle or stop-motion principle in the United States. The modality of this type seemed to have the capability to be a diagnostic tool, even if in some limited conditions (Fig. 12). However, it was still troublesome and inconvenient to search the heart, following an intracardiac structure.

In the upshot, the two-dimensional echocardiography based on the stop-action principle has not widely been used in the clinical setting. In general, although a clinical modality provides high-quality diagnostic information, simplicity in operation seems to be indispensable, so as to be used in routine.

What was described in Chapters I, II and III was about the circumstances of the cardiac ultrasound in the early 1960s and before. This period was not an age when some medical problems were solved by the ultrasonic diagnostics, but an age when diagnostics were newly created from the pulse reflection technique and/or the ultrasonic Doppler technique as materials in the technological sense. Therefore, in those days, cardiac ultrasound researches were not little interdisciplinary works. They were mostly original works, but were not yet widely known in medical circles.

IV. The Widespread Use of M-mode Echocardiography in the Late 1960s and Early 1970s — Age of M-mode echocardiography

Before 1965, M-mode echocardiography had been used only in some institutions, and the diseases which it could diagnose were limited, i.e., mitral stenosis, pericardial effusion, left atrial myxoma and so forth. In the late 1960s M-mode echocardiography began to spread in cardiology practice. The reasons for this spreading were considered to be that information on echocardiography slowly propagated, and that a new type of echocardiograph, which enabled one to directly monitor the M-mode image on a Braun tube screen, became commercially available. With this type of equipment, it became possible to search the inside of the heart, following the intracardiac structures on the image.
Utilities of echocardiography were fundamentally as follows:

(1) Analysis of morphology and motion of the heart. Echocardiography demonstrated some sort of diagnostic information on almost all heart diseases. It was particularly significant that echocardiography was useful in ischemic heart diseases [59-61]. This led to the idea of stress echocardiography later. Heart diseases which so far had been difficult to diagnose were easily diagnosed, i.e., mitral valve prolapse, rupture of chordae tendineae, hypertrophic cardiomyopathy and so forth. Moreover, even approaches to the complex congenital malformation became possible (Fig. 13).

(2) Measurement of heart size. Being derived from the size, some concepts related to cardiac function, i.e., cardiac output, circumferential shortening velocity, and so forth were obtained from the echo.

(3) Contrast echocardiography. Contrast echo had been performed since the early days of the echo [62]. At first, it was used for detecting shunts in congenital malformation. While the color Doppler infers the presence of shunt from the distribution of turbulence and of changes in flow velocity and flow direction, the contrast echo directly visualizes traveling of contrast material.

In the United States, many researchers rapidly gained so much experience in the echo, especially centering around Feigenbaum, Gramiak and so forth, that M-mode echocardiography seemed to have built up its own position in heart diagnosis around 1975, being characterized as “non-invasive”. It was called the “revolution of heart diagnosis.” In this sense the decade roughly from 1965 to 1975 is considered to be the age of M-mode echocardiography as the first generation of cardiac ultrasound in routine.

In Japan, some laboratories had been very active from the late 1960s. However the spreading of the echo into practice did not seem to be rapid. Here, let us observe the spreading of the echo from the aspect of the number of papers related to echocardiography presented in the scientific session at the Japanese College of Cardiology which developed in parallel with echocardiography (Fig. 14). The increase does not seem to be distinct from 1970 to 1974. In this period, while many cardiologists had been interested in the echo, some other doctors may have been prejudiced against the new modality. Although M-mode echocardiography visualizes intracardiac structure, the image is still a fairly abstract picture. In order to diagnose the

![Fig. 13.](image)

An example of diagnosis of complete transposition of great vessels by M-mode echocardiography (a ten-day-old baby, female)

A: Right to left M-mode scan at the level of heart base. Two semilunar valves are noted (RSL, LSL). They are sited in the manner of right-anterior and left-posterior. This result suggests transposition of great vessels.

B: Right to left M-mode scan at the level of atrioventricular valve. Two atrioventricular valves are noted (RAV, LAV). They are sited in the manner of right-anterior and left-posterior.

C: Base to apex M-mode scan. The left semilunar valve (LSL) switches over continuously to the left atrioventricular (LAV), so that this atrioventricular valve (LAV) is considered to be the mitral valve, and then the other atrioventricular valve (RAV) must be the tricuspid valve. According to the positional relationship between the two atrioventricular valves, this patient is considered to be d-loop. Van Praagh’s loop rule shows that in case of d-loop transposition of great vessels is mostly d-transposition, in which the aortic valve is sited right to the pulmonic valve. Therefore, the right semilunar valve (RSL) is considered to be the aortic valve and the left one (LSL) is the pulmonic valve in the present baby. The figure A reveals that the closing time is a little later in LSL than in RSL. This result also supports the above consideration. Then, the figure C also shows that the above determined pulmonary artery leads to the left ventricle and the aorta leads to the right ventricle. Finally, the present malformation is diagnosed as complete transposition of great vessels in d-loop and d-transposition. Further more, the figure C shows that the echo of the interatrial septum (IAS) is intermitted in the lower left part of the figure, that is, atrial septal defect is also present in this baby.
three-dimensional cardiac structure, which was based upon searching by a single ultrasound beam, some inference was further required for an examiner. This circumstance might be a reason for the above prejudice. The increase in 1975, '76, and '77 will show that the above mentioned barrier had been overcome. Values in 1978 and later are considered to be the result from the rapid spreading of real-time two-dimensional echocardiography.

V. Trials and Errors on the Way of the Development of Echocardiography

While “non-invasive visualization” of the intracardiac structure is an epoch-making progress of diagnostics obtained by echocardiography, on the contrary, identifying the echo source is sometimes considered to be difficult due to its “non-invasive” nature, resulting in a misinterpretation. This may be the predestination of “non-invasive.” Here, some consideration will be given on this point.

As mentioned before, the echo of the anterior mitral leaflet had been misinterpreted as that of the anterior wall of the left atrium for several years in the early stage of M-mode echocardiography[4]. In the latter half of the 1950s, nevertheless, M-mode echocardiography had been evaluated to be very helpful for diagnosing mitral stenosis[5-8]. The echo of the anterior wall of the left atrium at the start was corrected to that of the anterior mitral leaflet in 1961[10].

In the early days of contrast echocardiography contrast material was an indocyanine green solution[62]. The echo source was considered to be the coloring matter. However, in the middle of the 1970s a new view point gradually arose, whether or not the echo source was air microbubbles stealing into an injection system. As it is well known, at the present time, contrast material is a matter of bubble technology.

Furthermore, concerning the posterior wall of the left ventricle, in the late 1960s, a broad echo band at the pericardial side had been considered to show the whole posterior wall[63]. However, the endocardial surface really escaped notice (Fig. 15). This first came to be distinctly imaged in the middle of the 1970s. This item might be a matter of gain and image quality of the equipment used. Grey scale mode greatly contributed to the improvement of the image quality.

Similar difficulties in interpreting the echo source, such as those mentioned here, are not experienced only in M-mode echocardiography, but also in two-dimensional echocardiography. For example, the intima and midlayer of the coronary artery have been controversial in the intravascular ultrasound study.

The reasons for difficulties in interpreting the echo source are considered to be various. Some of them may be a matter of tissue structure; and some others, a matter of equipment used. Experimental study does not always seem to be easy. Persons concerned in echocardiography need to give serious consideration to their obtained results.
VI. Development of Two-dimensional Echocardiography — Establishment of Cardiac Ultrasound

The study of the ultrasono-cardio-tomography by Tanaka, Kikuchi and their coworkers\[52,53\], and those of two-dimensional echocardiography based on the stop-action principle by some other groups had been also continued during the age of M-mode echocardiography (Fig. 16). However these types of equipment finally did not become routinely used, mainly because of troublesomeness to operate. In parallel with their studies, studies of two-dimensional echocardiography with a high-speed scan system had been started from the late 1960s\[64,65\].

In 1973, N Bom and his coworkers\[66,67\] first devised a new linear array system for heart examination. However, it did not yet seem to be satisfactory in image quality. Within several years after that, various types of high-speed scan systems, i.e., phased array systems\[68-72\], high-speed mechanical scan systems\[73,74\], and so forth became commercially available.

There were arguments for a few years on merits and demerits of these types of systems for the heart. Since then, the phased array system has become the main trend in real-time two-dimensional echocardiography.

Real-time two-dimensional echo image was concrete and easy to understand. Intracardiac targets, which were apparently incomprehensive with the M-mode echocardiography, became often easily understandable with the real-time two-dimensional one (Fig.17). Prejudice against echocardiography was experienced in the case of the M-mode, but none in the case of real-time two-dimensional echo.

Advantages of real-time two-dimensional echocardiography were not only shortening of the recording time of each image and examination time, but also easy operation of a handy probe, and then, unexpectedly, enhancement of the capability to search the inside of the heart during monitoring real-time images of the intracardiac structures.

The above advantages were so great that real-time two-dimensional echocardiography was rapidly adopted into cardiac practice. It was the standard of cardiac ultrasound over the late 1970s and the early 1980s. Real-time two-dimensional echocardiography may be called the second generation of cardiac ultrasound in routine, if the M-mode one is called the first genera-
tion. Further, since 1980, it is routinely equipped with the pulsed Doppler system in combination.

(To be continued)

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