Short History of The Development of Echocardiography With Special Reference to That in Japan (2)*

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Continued from the last issue

Content of this article

I. Introduction of the ultrasonic reflection technique into cardiac diagnostics.

II. The dawn of the ultrasonic Doppler diagnostics in the cardiovascular field.

III. Contributions of Japanese researchers to the cardiac ultrasound in early 1960s.

1) Correspondence between the echo- and the Doppler cardiograms

2) Ultrasonic intravenous sonde.

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

IV. The widespread use of M-mode echocardiography in the late 1960s and early 1970s —— the age of M-mode echocardiography.

V. Trials and errors on the way of the development of echocardiography.

VI. Development of two-dimensional echocardiography —— Establishment of cardiac ultrasound.

VII. Approaches to Intracardiac Blood Flow and The Development of Pulsed Doppler Technique

In the late 1960s and the early 1970s, while the cardiac Doppler was rapidly spread for the early diagnosis of pregnancy [75-77], it was not for the heart diagnosis of an adult. People might have been more interested in the cardiac echocardiography than in the cardiac Doppler, because the image was more concrete in the former than in the latter. In the same period as that mentioned above, the blood flow Doppler was used for studying brain circulation [30, 31, 78] and peripheral circulation [79, 80], but not for the intracardiac flow. In those days, the original type of Doppler technique used continuous ultrasound beam. In this case, it was considered to be difficult to analyze the intracardiac flow condition, because the intracardiac flow might be complicated by variously directed flows, and the continuous wave ultrasound could not separately recognize each variously directed flows.

In spite of these circumstances, D. Kalmanson and coworkers analyzed cardiac output and venous return in 1968, measuring the carotid and jugular flows transcutaneously with the directional Doppler technique [81]. The following year, they studied right-cardiac flow with the Doppler catheter, and then the left-cardiac one by the transseptal approach. (Fig. 18) [82, 83]. About the same time, A. Benchimol and coworkers also studied intracardiac flow and coronary flow with the Doppler catheter. Because a catheter tip transducer picks up the Doppler output only from a small volume near the transducer due to its small size, the difficulty mentioned above is considered to be by and large avoided.

Further, the above catheter studies, generally speak-
ing, seemed to include a new idea to bring a probe close to a site of interest in the body, giving up the concept "noninvasive" which had been the most specific feature of ultrasound diagnostics. It might be worthy of attention that such a new idea already appeared in the early days of the cardiac ultrasound. This idea may have lead to the progress of the intravascular ultrasound in the 1980s (See Chapter IX).

In order to noninvasively assess the intracardiac blood flow, it had been desired to develop a range-gated Doppler technique in the late 1960s.

Around 1970, the pulsed Doppler technique was developed by D.W. Baker [86], P.N.T. Wells [87], and P. Peronneau [88] independently from each other. Baker had been studying this technique under the supervision of J. Reid [89]. In Japan, M. Okujima, S. Otsuki, and coworkers [90] devised the M-sequence modulated Doppler flow velocity-meter for the same purpose as that of the formers. After the appearance of the new technique, the original type of Doppler technique was called the continuous wave Doppler technique (CW-Doppler technique).

The purpose of the new Doppler technique was to obtain a velocity profile of blood flow in a vessel [91]. However, researchers gradually began to direct their interest to the intracardiac flow [92]. Tanaka and coworkers [93] had already obtained the velocity profile of the left ventricular outflow tract with the M-sequence modulated Doppler technique, superimposing the beam directions on their own type of two-dimensional echo image (Fig. 19).

When the pulsed Doppler technique was applied for the intracardiac flow and deep vessels, it had to be inevitably linked with the echo technique for monitoring the site of sample volume [92]. There had been some intermediary types of linkage [93-98] (Figs. 20 and 21). After all, as seen in the present time, the pulsed Doppler system was usually combined to the real-time two-dimensional echocardiography with a single transducer which enabled one to operate both systems simultaneously.

At this time some comments should be given on significance of the display system of Doppler output (Fig. 22). In the early stage of blood flow Doppler a frequen-
cy discriminator and an electromagnetic oscillograph had been used for the display. Then, a zero-cross counter had been widely used for the peripheral vessels for a long time. It nearly shows mean velocity in a cross-section of a vessel. It can not separate the forward and reverse flows, but can show the sum of them. So, it did not seem to be adequate for assessing the intracardiac flow.

In some laboratories in Japan and Europe, off-line frequency spectrographs of heterodyne types have been used from the early stage of the Doppler. In this case, an envelope of waves, formed on the spectrogram, shows a temporal change of the instantaneous peak velocity in a cross-section of the vessel. Because the visual pattern on the spectrogram was generally easy to understand, it was often very helpful for clinical phenomena in practice (Fig. 23). Since high-speed Fourier analysis with a line-scan recorder became available around 1975, it has been exclusively used for the real-time display of the flow Doppler. The real-time mode is an indispensable feature to search the heart interior for the cardiac Doppler as well as the cardiac echo.

Let’s return to the combination system of the pulsed Doppler technique and real-time two-dimensional echocardiography. The combination system was usually equipped with the above mentioned real-time display system for the flow Doppler, so that the combination system enabled one to search the heart very efficiently. The new combination technique has been called “Doppler-echocardiography,” and has been very

Fig. 20.
An example of intermediary types of the combination of the pulsed Doppler system and the echo image: the pulsed Doppler system and the echo image by the contact compound scan based on the stop action principle [94, 95].

Right top: After recording the left ventricular long axis section, the probe for the echo was replaced with that for the Doppler, then the beam directions for the Doppler (white lines A and B) were recorded, being superimposed on the echo image. Small white squares show site of sample volumes.

Right bottom: schema
Left: time-sequential flow patterns on each sample volumes. Numeral shows depth of the sample volume from the transducer. In mid-diastole (black arrows) According to the flow patterns presented here, it may be considered that left ventricular inflow runs along the ventricular wall in mid-diastole, rather than being subject to mixing in the left ventricular cavity, as shown in the schema.
(Present author’s laboratory, 1976)

Fig. 21.
Another example of intermediary types of the combination: Two-probe type [98]. one for the phased array and the other for the pulsed Doppler, were connected by two potentiometers. The positional relation between the image of the heart structure and the Doppler beam on the screen is controlled by these potentiometers.

In the figure, a black probe is for the phased array, and the white one is for the pulsed Doppler.

In general, a beam direction for imaging heart structure is not necessarily convenient for the Doppler examination. The reverse is also true. The present type of combination may avoid the above-mentioned shortage. However, the present type is rather difficult to operate.

(Trial manufacture by Hitachi Medico, 1977)
rapidly spread over the field of cardiology. Here, the
number of papers related to the pulsed Doppler tech-
nique in the Scientific Sessions of Japan Society of
Ultrasonics in Medicine (including M-sequence
Doppler flowmetry) from 1970 to 1982 is shown (Fig.
24). The rapid increase after 1980 has been due to the
widespread of Doppler-echocardiography in Japan.
Thus, Doppler-echocardiography has been a standard
type of the cardiac ultrasound in the early 1980s.

From the pathophysiological aspects of heart dis-
ease on the macroscopic level, static and dynamic
states of the intracardiac structures are conceptually
inseparable from the intracardiac flow conditions. The
significance of Doppler echocardiography is that this
new technique enables one to conjunctionally assess
the structure and flow of the heart in the clinical set-
ing. In this sense, Doppler-echocardiography might
be apparently considered as “finished goods.” Howev-
er, it has had still some shortcomings. For example,
while the structure information was recorded in the
two-dimensional image, the flow information was dis-
played in time-sequential form. This did not necessarily
seem convenient in the clinical setting. So, further
progress was desired for the Doppler-echocardiogra-

Fig. 22.
Intermediary types of display for the blood flow Doppler
Top: Frequency discriminator and electromagnetic oscillograph The out-
put from this modality is proportional to frequency, so that the
envelope of the output is similar to those of other two types. At
the start of the Doppler study this type was exclusively used.
(See Figs 3-6)

Middle: Zero-cross counter
The output of this modality does not show instantaneous mean
velocity in the beam, but shows a value near it. This modality is
simple and inexpensive. Therefore, this has been rather widely
used for examining peripheral blood flow. However, when for-
ward flow component and reverse one coexist simultaneously in
a flow, this modality can not separate them, but shows their sum-
mation.

Bottom: Frequency spectrogram: The envelope of this out put shows
temporal change of instantaneous peak velocity. In the early days
of the Doppler study it was based on heterodyne principle and
used off-line. At the present time it is based on the high-speed
Fourier analysis and used on-line.

Fig. 23.
Flow patterns of the common carotid artery, displayed by a fre-
quency spectrograph of hetero-
dyne type, in some cardiac disor-
ders with ejection abnormalities.
Left top: healthy subject
Right top: mitral regurgitation
Left middle: hypertrophic obstruc-
tive cardiomyopathy
Right middle: aortic regurgitation
Left bottom: pulsus alternans
Right bottom: aortic stenosis
(The present author’s laboratory)
phy.

Around 1985 the color Doppler system was developed [98-100]. It was so rapidly adopted in the field of cardiology that it became the standard in cardiac ultrasound, taking the place of conventional Doppler echocardiography. This shift may be called the third generation of the cardiac ultrasound in routine [101, 102]. Thus, the cardiac ultrasound has entered the present age from history.

VIII. Connection of Cardiac Ultrasound with Hemodynamics, and Reevaluation of the Continuous Wave Doppler Technique in the Assessment of Intracardiac Blood Flow

Other remarkable progresses in the age of Doppler-echocardiography around 1980 were that CW-Doppler technique (continuous wave Doppler technique) became available for measuring the intracardiac blood flow in some limited occasions, and that Doppler-echocardiography was numerically connected with hemodynamics.

Let’s take up the first subject. Among the intracardiac flows, some particular ones, e. g., regurgitant flow, post-stenotic flow, and so forth, are remarkably speedy and easy to estimate their localization, referring to the anatomy and their high-pitched Doppler tone. They seem to be easily discriminated from other flows because of their high velocity [103, 104]. Therefore, if the peak velocity of a velocity wave only is required, it may not be necessarily obtained by the pulsed Doppler, but by the CW-Doppler only. In this case, of course, it is required to search the cardiac chamber, monitoring flow patterns in real-time on the display as aforementioned. Detection is often possible only by hearing the high-pitched Doppler tone due to the high flow velocity.

According to this process, the CW-Doppler technique has been adopted for assessing the intracardiac flow in parallel with the pulsed Doppler, even if this has been limited in some particular flows.

Let’s enter into the latter subject. According to fluid dynamics, the following equation, i. e., the Bernoulli equation, holds true for a certain flow:

\[
p_1 - p_2 = \frac{1}{2} \left( v_1^2 - v_2^2 \right)
\]

Here, \(p_1\) and \(v_1\) are pressure and flow velocity at Site (1), respectively, and \(p_2\) and \(v_2\) at Site (2), and \(\rho\) is the density of the fluid. If the units are mmHg for \(p\) and m/sec for \(v\), respectively, and \(\rho\) is nearly equal to 1:

\[
p_1 - p_2 = 4\left( v_1^2 - v_2^2 \right)
\]

approximately holds true. Furthermore, if \(p_2\) and \(v_2\) are small and negligible in comparison with \(p_1\) and \(v_1\), respectively, the above equation is written as below:

\[
p = 4v^2
\]

This equation is called the simplified Bernoulli equation. It is considered to be approximately applicable to the intracardiac flow, e. g., regurgitant flow, post-stenotic flow, and so forth. Thus, the above relationship between \(p\) and \(v\) first connects cardiac ultrasound (Doppler velocity) with hemodynamics (pressure) numerically [105].

So far, ultrasound had provided information mainly on organ structure. The above relationship enabled one to estimate intracardiac pressure, i. e., the pressure gradient at stenosis [103, 105-107], left atrial pressure, pulmonary artery systolic pressure [108], and so forth, measuring intracardiac flows concerned by the cardiac Doppler. Although the above consideration on the relationship between \(p\) and \(v\) did not include any new concepts in fluid dynamics, the connection between cardiac ultrasound and hemodynamics was an
epoch-making progress from the aspect of ultrasound diagnostics.

**IX. Diversification in the Usage of Cardiac Ultrasound in the Age of Two-dimensional Echocardiography**

It was another characteristic feature of the age of two-dimensional echocardiography, with and without Doppler function, between 1975 and 1985, that a new trend of diversification appeared in the usage of cardiac ultrasound. Generally speaking, this new trend might have resulted from a background that knowledge on ultrasound diagnostics had been widely propagated in medicine and related fields, and that many people in these fields had become interested in cardiac ultrasound.

In general, it is often difficult to obtain information of good quality on the cardiac structures, especially on the left ventricle, in case of obesity, pulmonary emphyseum, senility and so forth. In 1976, in order to overcome this difficulty, L. Frazin and coworkers [109] attempted the transesophageal approach with their special M-mode probe. They could obtain M-mode records in more patients with this approach than with the conventional anterior-thoracic approach. In 1977, M. Matsuzaki and coworkers [110-113] succeeded in a transesophageal approach with a probe, in which an ultrasound transducer was mounted on the tip of a gastroscope. They used at first the M-mode and then the phased array. In the same year, K. Hisanaga and coworkers [113-115] also reported their own type of transesophageal approach, a high-speed mechanical scan, using the gastroscope structure. It was noteworthy that although Hisanaga was a physician, his transesophageal probe was his own creation. Transesophageal transducers were generalized and then improved.

Transesophageal echocardiography had been mainly used at first for intraoperative monitoring of the left ventricular function [116]. Then, however, it became widely used because of its usefulness, and, as observed at present, has been established as a special field in echocardiography.

The transesophageal approach had been once attempted in the early 1960s (See Chapter III 2)). However at that time it had been fruitless [43-47]. The reason for this fruitlessness might be difficulty in making a helpful probe. The successes were in the late 1970s with the gastroscope structure. Generally speaking, it may need progression of applicable techniques, as well as a good conception, to develop the cardiac ultrasound. In other words, on developing ultrasound diagnostics it should be taken into consideration that even a new idea which has been once difficult to be realized may often become realized with the progress of related applicable techniques. Similar circumstances are experienced concerning the Doppler signal of the heart wall. It was left as unavailing in the early stages of the cardiac ultrasound, because there was no helpful technique to analyze it. However, it is now utilized for heart diagnosis by the tissue Doppler imaging (See Chapter II).

Let’s go forward to next topic. In 1985, R. F. Wilson and coworkers [116] measured coronary flow velocity with a Doppler catheter, then estimating coronary reserve as well. Regarding studies with Doppler catheters, there had been detailed studies by Kalmanson and coworkers on intracardiac flow [81-83] and then those by Benchimol and coworker [84, 85] in the late 1960s and early 1970s. There has been no active study following them until Wilson’s study. However, following Wilson’s study with the Doppler catheter, a variety of internal approaches, i.e., Doppler guide wire, some kinds of IVUS, and so forth successively appeared in the 1990s and were rapidly adopted in cardiology. These internal approaches, including the transesophageal approach, have been based that one brings a transducer close to the region of interest sited deeply into the body in order to obtain high-quality information, even more or less at the cost of “non-invasive.” At present, the capability of internal approach becomes one of the characteristic features of the ultrasound diagnostics in parallel with “non-invasive” (See Chapter VII).

Here, it should be pointed out that the development of new modalities generally is under the influence of medical circumstances at the time. Namely, the appearance of a lot of new internal approaches might be considered to be tacitly promoted by the progress of coronary interventional therapies. In the past, M-mode echocardiography might have been also originat ed against the background of the development of valve surgery.

Contrast echocardiography had been already used since the early days of echocardiography [62]. As mentioned above, the first contrast material was an indocyanine green solution. However, slowly it had been recognized that the contrast echo source was not
the coloring matter, but the air bubbles contaminating
the injection system. Since those days, microbubbles
have been made of saline, glucose solution, human
albumin solution, contrast material for X-ray examina-
tion, and so forth. Contrast echocardiography has
been applied for imaging of blood flow, diagnosing
genital malformation, identifying endocardial sur-
face, enhancing the Doppler signal, etc. However peo-
ples specialized in contrast echocardiography have
been interested in the visualization of myocardial perfu-
sion [116-120]. This new trend might have been due
to the influence of the progress of coronary interven-
tional therapies. Then, contrast echocardiography
reached a new situation.

As well known, an intravenously-injected former con-
trast material could not pass through the pulmonary
capillary system, and could not opacify the left ventric-
ular cavity and, of course, the myocardium. In order to
search the myocardium, the contrast material had to
be directly injected into the coronary artery. There-
fore, a new contrast material was desired, which can
occlude the left ventricular cavity and then the
myocardium, being intravenously injected and passing
through the pulmonary capillary system. In order to
produce such a contrast material mentioned above, it
has been handed over to the next age, i. e., to the pre-
sent time, to elucidate fate of contrast bubble, interac-
tion between bubble and tissue, that between bubble
and ultrasound as well as substances of bubble wall,
kinds of embedded gas, and process of manufacture.

Further, stress echocardiography and intraoperative
echocardiography had already been performed in the
age of two-dimensional echocardiography [121-126],
between 1975-1985, and then developed into important
fields of cardiac ultrasound in the clinical setting at the
present time.

Now cardiac ultrasound is showing a new trend of
diversification; a lot of new usages and techniques are
successively developed, that is, transesophageal
echocardiography, stress-echocardiography, intravas-
cular ultrasound, new contrast materials, three dimen-
sional echocardiography, tissue characterization, tis-
sue Doppler imaging, harmonic imaging, etc. The
foremost signs of the new trend have already appeared
in the last age of two-dimensional echocardiography,
between 1975-1985. In this sense, the period extend-
ing over the last age and the present time may be
called, in the future, the second dawn of the cardiac
ultrasound.

In conclusion

The study to introduce the ultrasound reflection
technique into cardiology began in 1953, and in 1955
the ultrasonic Doppler technique. A period of about
ten years before 1965 was the dawn of ultrasound diag-
nostics of the heart. In this age, there were not many
attempts to use ultrasound for heart diagnostics
besides the above mentioned techniques.

In next age, i. e., the period from 1965 to 1975, M-
mode echocardiography was the leading type of car-
diac ultrasound. It was the first generation of ultra-
sound diagnostics of the heart in routine. This period
may be called the age of M-mode echocardiography.
In the period from 1975 to 1985, the leading type was
real-time two-dimensional echocardiography with and
without Doppler function which was the second gener-
ation in routine. This period may be called the age of
two-dimensional echocardiography. The period from
1985 to the present time may be called the age of color
Doppler, which has been the third generation of the
cardiac ultrasound in routine.

However, since the middle of the last age, cardiac
ultrasound has been showing the diversification of
techniques and usages. Therefore, it is uncertain
whether the age division as such can be continued.
The period extending over the latter half of the last age
and the present time may become the second dawn of
the cardiac ultrasound.

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