HISTORY OF DOPPLER ULTRASOUND

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I. HISTORICAL BACKGROUND

Doppler ultrasound involves measurement of the velocities of blood or tissues by the Doppler principle. The Doppler effect concerns the change in perceived frequency by an observer of a wave as a result of motion of either the source or observer or both. This effect, which was subsequently named after him, was proposed by the Austrian physicist Johann Christian Doppler in 1842 [1], to explain the colour of binary stars. The now classic Doppler equation was deduced:

$$f_o = f_s \left(\frac{c-v_o}{c-v_s}\right) \quad (1)$$

where f_o is the frequency perceived by the observer, f_s is the frequency emitted by the source, c is the wave speed in a stationary medium, v_o is the vector velocity of the observer and v_s the vector velocity of the source.

In fact the effect proposed by Christian Doppler was too small to explain the colour of stars. However the effect was shown to be valid for sound by the Dutch physicist Christophorus Buys-Ballot in 1845. His experiment involved a group of musicians playing on a moving train, with stationary observers on the ground as the train passed. Subsequent work has confirmed that the Doppler effect is valid for any wave, including sound, electromagnetic (radio, microwave, light etc.) and gravitational waves. Figure 1 illustrates the Doppler effect. Further reading of Christian Doppler and early work on the Doppler effect may be found in review articles [2-3].

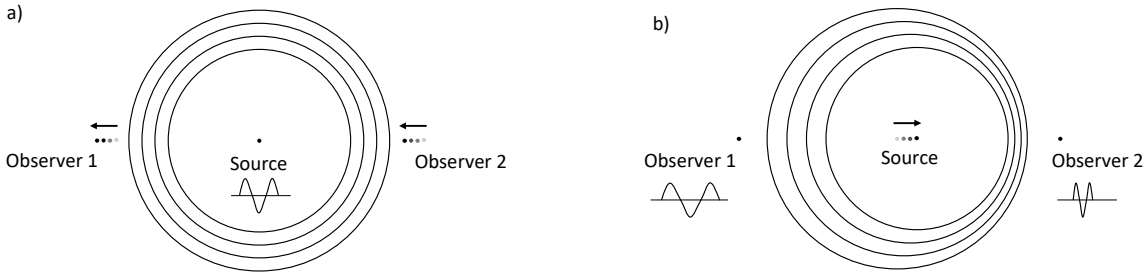

Fig. 1. Doppler effect; there is relative movement between the source and the 2 observers. a) Wave motion with respect to the source. The wave propagates symmetrically in all directions at a frequency *f*. b) Wave motion with respect to the observers. Wave propagation is asymmetric; there is contraction of the wave as perceived by Observer 2 who perceives a higher frequency (f_2>f); for Observer 1 there is dilation of the wave who perceives a lower frequency (f_1<f).

II. EARLY DOPPLER ULTRASOUND

The first medical investigations using the Doppler effect were undertaken by Shigeo Satomura from the Institute of Scientific and Industrial Research of Osaka University in Japan. Working in the area of industrial radar and ultrasound he was encouraged by his supervisor Kinjiro Okabe to investigate medical applications. Satomura's first studies were actually not on blood flow, but on cardiac motion, and therefore the first Doppler ultrasound paper is also the first Tissue Doppler paper. The paper published in 1956 in Japanese was titled 'A new method of the mechanical vibration measurement and its application' [4] A follow-up paper was published in English in 1957 [5]. The Doppler device used a 3 MHz continuous wave probe with a central transmit element surrounded by a ring shaped receive element. The receive signal was demodulated and band-pass filtered from 500-1500 Hz. The Doppler signal was displayed as an amplitude signal along with the ECG and cardiac sounds (Fig. 2). These 2 papers show for the first time the now widely used Doppler equation:

$$f_d = 2\frac{v_o}{\lambda} \quad (2)$$

where f_d is the Doppler frequency, v_o is the velocity component along the ultrasound beam and λ is the wavelength.

Noting that:

$$c = f\lambda \quad (3)$$

where f is the transmit frequency and c is the speed of sound, equation (2) can be rearranged to give the modern version of the Doppler equation as applied to medical ultrasound, assuming that transmit and receive beams are aligned:

$$f_d = \frac{2fv\cos\theta}{c} \quad (4)$$

where θ is the angle between the beam and the direction of motion.

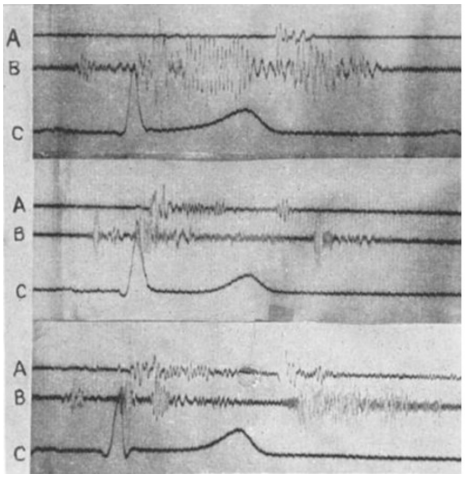

Fig. 2. Oscillograms obtained by Satomura (1957) from the heart. A: Heart sounds, B: Doppler signal, C: ECG. Reproduced from ; Satomura S. Ultrasonic Doppler method for the inspection of cardiac functions. J Acoust Soc Am1957;29:1181-1185, with permission of the Acoustical Society of America.

In a review paper [7] on early Doppler development it was noted that Satomura and his colleagues identified 2 types of Doppler signal from the heart; those with frequencies below 500 Hz which were thought to arise from heart wall motion and one at 1000 Hz which was thought to arise from valve motion. The first paper reporting detection of blood flow was published by Satomura in a 1959 paper titled 'Study of the flow patterns in peripheral arteries by ultrasonics' [6]. Doppler signals were obtained from water flowing in a tube, and also for flow in the brachial artery and vein (Fig. 3).

The 2 papers by Satomura in 1956 and 1959 represent the first studies of Doppler ultrasound in humans. Satomura went on to develop the 'Ultrasonic Blood Rheograph'. The Rheograph was the first commercial ultrasonic Doppler flowmeter, manufactured by the Nippon Electric Company (NEC) and available from 1959 (Fig. 4). Tragically Shigeo Satomura died of a subarachnoid haemorrhage in April 1960. The work on the Rheograph system was presented by his colleague Ziro Kaneko at the Third International Conference on Medical Electronics in the same year [8].

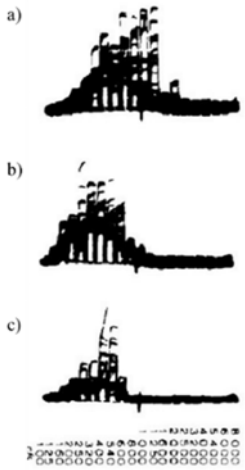

Fig. 3. Frequency spectra obtained from: a) brachial artery systole, b) brachial artery diastole, c) brachial vein. Reproduced from Ultrasound Med Biol, Vol. no. 12, Kaneko Z, First steps in the development of the Doppler flowmeter, pp. 187-195, copyright Elsevier (1986).

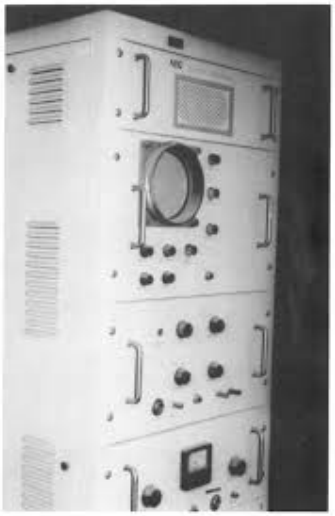

Fig. 4. First commercial Doppler ultrasound system; the 'Blood Rheograph' available in 1959 and developed by the Nippon Electric Company (Japan). Reproduced from Ultrasound Med Biol, Vol. no. 12, Kaneko Z, First steps in the development of the Doppler flowmeter, pp. 187-195, copyright Elsevier (1986).

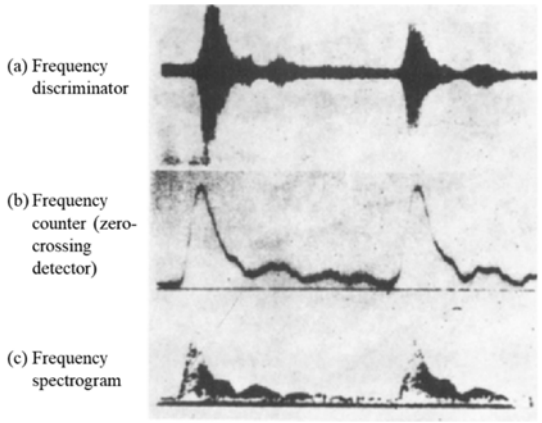

Fig. 5. Blood flow patterns in the brachial artery registered by 3 methods. Reproduced from Ultrasound Med Biol, Vol. no. 12, Kaneko Z, First steps in the development of the Doppler flowmeter, pp. 187-195, copyright Elsevier (1986).

Satomura's work was carried on by colleagues and a number of developments were made. There was the realisation that the Doppler signal from blood did not arise from turbulence but from red cells, and that the Doppler frequency was correlated with blood velocity [9]. It was recognised that the recording system was a critical component and several different methods were developed (Fig. 5). A frequency discriminator recorded voltages below a set value of 1000 or 2000 Hz. Use of a zero-crossing detector was also attempted [10]. This method, which became popular in early Doppler, was dismissed by the Osaka group as it suffered from interference from low frequency noises present in clinical studies. The final and preferred method was spectral display consisting of a Doppler frequency - time trace [11]. A method of Doppler detection was developed which allowed the Doppler signals arising from forward and reverse flow to be separated [12].

The paper by Kaneko [7] provides more details of the early development of the Doppler flowmeter.

III. Continuous wave (CW) doppler

The first CW Doppler systems were 'blind' in that there was no accompanying B-mode image. The transducers were typically designed in a split-D format with adjacent transmit and receive elements or followed the Satomura approach of a central circular transmit element with a surrounding receive ring element.

Compact non-directional CW Doppler systems were described by the group from the University of Washington in Seattle [13-16]. This followed from work by the same group on the development of invasive probes for measurement of flow in arteries [17-18]. The Doppler output was in the form of an audible signal generated from a zero-crossing detector where hardcopy recordings of the Doppler trace could be made through connection to a chart recorder. Recordings were made of flow in arteries in the upper and lower limbs, carotid arteries and aorta.

In addition the first waveforms during pregnancy were recorded, from the uterine artery and vein, and from the fetus; figure 8 in the 1966 paper by Rushmer [15] identifies 'fetal flow' which looks to be from the fetal aorta.

The compact CW Doppler described in 1966 by Rushmer [15] was the forerunner of the 'pocket Doppler'. It soon became apparent that there was a wealth of information in the audible signal which the operator could use to identify normal from abnormal flow in disease. The small size, low cost and clinical utility helped to spread pocket Doppler in hospitals. Over 50 years later the design of pocket Doppler is virtually unchanged from that described by Rushmer et al; continuous-wave non-directional with audio output and can easily fit in a coat pocket.

Fig. 6. Doptone CW Doppler system manufactured by the Smith-Kline Instrument Company (Philadelphia, USA). The system was the first fetal heart monitor. The version illustrated was used in peripheral vascular applications. Reproduced with permission from the British Medical Ultrasound Society.

Recordings of Doppler from the fetal heart were reported by Callaghan in 1964 [19] and Johnson et al. in 1965 [14]. The CW Doppler system developed by the Seattle group was commercialised by Smith-Kline Instrument Company (Philadelphia, USA) as the 'Doptone' in 1965 (Fig. 6), which was used for fetal heart detection [20] and for applications in the peripheral vascular system [21].

Subsequent developments paralleled work done in Japan. Directional detection was developed by McLeod in 1967 [22] where audio signals from forward and reverse flow were available as separate audio channels, e.g. using stereo headphones. Single-line display was developed using a zero-crossing detector, and later spectral Doppler display was implemented [23]. The latter involved recording the Doppler signals on magnetic tapes and sending them to Northrop Nortronics (Needham Heights, USA) and waiting 6 weeks for the results [24].

The basis of the original quadrature detector developed by McLeod involved splitting the Doppler signal into 2 paths, phase shifting one channel by 90º to create a direct (D) and a quadrature (Q) signals, and comparing the phase lag between the D and Q signals. Depending on the lag the signal could be switched to either the forward or reverse channel. This system suffered from switching artefacts and for flow in which there was simultaneous forward and reverse flow the flow direction could not be resolved. Later developments overcame these limitations and are described by Coghlan and Taylor in 1976 [25].

The zero crossing detector was widely used in early Doppler systems. The detector in its simplest form produces a signal every time the display goes from negative to positive. With no noise and no offset the output from the zero-crossing detector should be equal to the mean (RMS) Doppler frequency [26]. Noise produces a large number of false crossings, and in practice an offset threshold is implemented using a set-reset procedure; that is a trigger is set if the amplitude exceeds a positive threshold value, and the trigger is reset when the amplitude exceeds a negative threshold value. In this way noise has limited effect and the system is able to provide an output proportional to frequency [27]. Single-line Doppler displays were phased out following the introduction of real-time spectral display as described in the next paragraph.

Early Doppler spectral analysis was performed off-line, commonly using a swept-filter system. Sound spectrographs were developed during World War 2 to help analyse enemy messages [28]. Subsequently sound spectrographs were used in speech therapy and in the recording of bird songs. In the Kay Spectrograph (Kay Electric Company, Pine Brook, USA), charge sensitive paper was attached to a rotating drum (Fig. 7). As the drum rotated the Doppler signal was filtered by a narrow band filter which scanned the frequency range increasing from negative to positive frequencies. The pen touched the paper when there was signal. A two second spectrograph was produced in around 2 minutes. The advent of real-time spectrum analysis [29-33] allowed this feature to be incorporated into commercial systems. The availability of Doppler spectral data opened up the field of Doppler waveform analysis which is discussed in the next section.

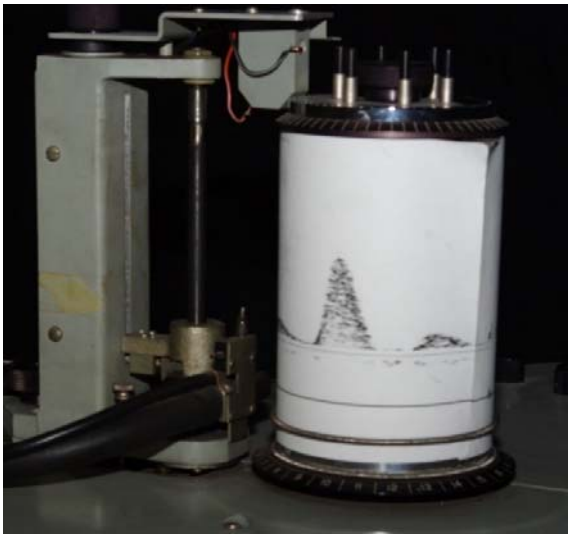

Fig. 7. Spectral Doppler tracing made by the Kay Spectrograph (Kay Electric Company, Pine Brook, USA). The tracing is in-place on the paper attached to the recording drum of the machine. Reproduced with permission from the British Medical Ultrasound Society.

In peripheral arteries CW Doppler was used to evaluate the extent and location of arterial disease. Local increases in Doppler frequency occurring as result of stenosis could easily be observed by tracking the transducer along the artery. Peripheral arteries are approximately parallel to the surface, so even though the exact beam-vessel angle is unknown provided that a similar beam-skin angle is adopted the Doppler frequency data could be compared between patients. Spencer and Reid in 1972 [34] demonstrated the increase in maximum frequency with degree of stenosis in carotid arteries. Most quantification involving flow waveforms from CW Doppler has involved quantities related to waveform shape as discussed in section IV.

In cardiology stand-alone CW Doppler was used to measure the flow waveform from the ascending aorta, as an indicator of cardiac output [35]. The transducer was placed on the suprasternal notch and angled down and to the left; the blood flow in the aorta was approximately parallel to the beam axis at this position. The device was subsequently commercially marketed as the 'Transcutaneous Aortovelograph' (Muirhead Medical Ltd, Beckenham, Kent, UK).

CW Doppler had limited clinical impact in cardiology [36], however Feigenbaum [37] notes 'The breakthrough came when Holen then Hatle demonstrated that haemodynamic data could be accurately determined with Doppler ultrasound'. Both groups used CW Doppler to acquire velocity data from which pressure gradient was calculated [38-41], further discussed in section IX. Gradually stand- alone CW Doppler systems became redundant with the widespread availability of duplex then colour flow Doppler systems.

Further reading on the history of CW Doppler may be found in review articles [42-45].

IV. Waveform analysis

The absence of B-mode imaging meant that stand-alone CW Doppler systems were mainly used in arteries with defined locations and/or defined waveform shapes. Early applications were therefore in the lower and upper limbs and in extra-cranial arteries. The abdomen and fetus were difficult as there are many arteries with similar waveform shapes and there was no easy way of distinguishing from which vessel the Doppler signal arose.

The other limiting feature of stand-alone CW Doppler is the lack of knowledge of the angle θ between the beam and direction of motion. Conversion from Doppler frequency shift to velocity, commonly practiced using duplex Doppler (see below), requires knowledge of the angle θ so is not possible using stand-alone CW Doppler. Quantification of the Doppler waveforms from stand-alone CW Doppler therefore relied on indices related to the Doppler frequency (e.g. maximum Doppler frequency) or indices of waveform shape. As the Doppler signal varies linearly with velocity, indices of waveform shape should (at least in principle) be independent of the angle θ. Some indices of waveform shape are described below and illustrated in Fig. 8.

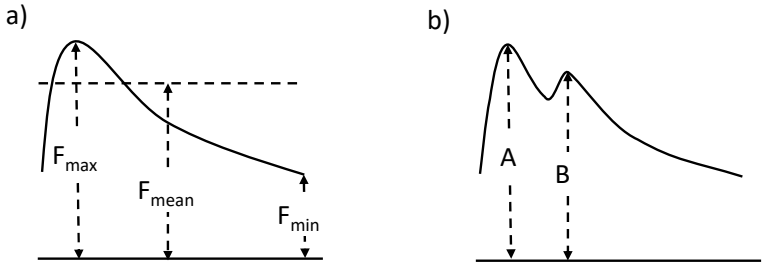

Fig. 8. Waveform indices. a) Measurements relevant to RI and PI. b) Measurements relevant to the A/B ratio.

Pulsatility index (PI). Early studies using CW Doppler observed that there was considerable variation in the degree of diastolic flow in arteries. Arteries supplying muscle at rest (eg. femoral, brachial) were highly pulsatile with little reverse flow while others (carotid arteries) exhibited a high degree of diastolic flow. Doppler waveforms distal to an arterial stenosis lost pulsatility. In its original formulation by Gosling and King in 1969 [46] PI was defined in terms of Fourier components but was later simplified [47] (Fig 8a) to:

$$PI = \frac{F_{max} - F_{min}}{F_{mean}} \tag{5}$$

Resistance index (RI). The RI also quantifies the degree of diastolic flow. This was developed by Pourcelot in 1974 [48] and is defined (Fig. 8a) as:

$$RI = \frac{F_{max} - F_{min}}{F_{max}} \tag{6}$$

A/B ratio. It was noted that waveforms from the carotid arteries and supraorbital arteries have a second peak whose height increases when there is major carotid atherosclerosis. The A/B ratio was therefore defined as the height of the major systolic peak divided by the height of the secondary peak [47], Fig. 8b. In practice not all waveforms have a clearly distinguishable second peak making this index impossible to calculate in all patients.

The above indices are measured from a single trace; so from the zero-crossing output when there is no spectral display, or from either the mean or maximum Doppler frequency when there is spectral display.

The availability of spectral display offered new possibilities for quantifying waveforms. In particular it was noticed that there was a difference between the waveforms from normal and diseased arteries. Normal arteries have a 'window' beneath the outer maximum Doppler shift where there is little data, as most of the velocities in the Doppler sample volume are travelling at similar velocities. In diseased arteries there is loss of this window as a result of turbulence. Several studies have developed indices which quantify the degree of broadening, reviewed in the book by Evans et al. on page 173 [49]. All the indices have the same intent so only a few are shown below:

$$SB = \frac{F_{max} - F_{min}}{F_{max}} \quad \text{(Johnston et al. 1981, [50])} \tag{7}$$

$$SB = \frac{F_{min}}{F_{max}} \quad \text{(Rittgers et al. 1983, [51])} \tag{8}$$

$$SB = \frac{F_{max}}{F_{mean}} \quad \text{(Sheldon et al. 1983, [52])} \tag{9}$$

In fact there are many sources of spectral broadening other than disease which makes it difficult to compare studies.

Other more complex forms of waveform analysis were explored. Laplace Transform Damping developed by Skidmore et al [53-55] was applied to the maximum Doppler frequency waveform from arteries of the lower limb. The method modelled the artery as a simple equivalent circuit and extracted parameters related to stiffness, distal impedance and diameter. However the model was unrealistic in that it constrained the waveform to start at zero flow which was unrealistic, and it did not account for the large components of reflected waves seen in disease. Principal component analysis is a generic method which breaks down the data into a number of base components, similar to Fourier analysis. This was applied to the whole Doppler spectrum from arteries in the lower limb, treating the Doppler spectrum as an image [56,57]. These more complex methods have not passed into clinical practice.

Research into waveform analysis has continued up to 2020. However the main work in this area was undertaken in the 1960s-1980s and there has been little progress since that time. Waveform analysis was superseded by the area of velocity measurement (section IX), enabled by the advent of duplex Doppler (section VII). Further reading on waveform analysis is provided in reviews [49,58].

V. Pulsed wave (PW) doppler

For CW Doppler the sensitive area arises from the cross-over of the transmit and receive beams. There may be 2 or more vessels within the sensitive region, and the exact depth from which signals arises is not known. The impetus for pulsed wave Doppler came from the need to control the depth from which Doppler signals arose. Pulsed wave Doppler systems were developed contemporaneously by Baker et al (1967, 1970), Peronneau and Leger (1969), Wells (1969) and Flaherty and Strauts (1969) [59-63]. Later Angelsen (1975, 1976) [64,65] developed a combined PW/CW Doppler unit PEDOF (Pulsed Echo Doppler Flowmeter), marketed by Vingmed (Horten, Norway). A later version of the device was marketed in 1981 as ALFRED (All Frequency Doppler).

Stand-alone PW Doppler systems did not gain the same clinical acceptance as stand-alone CW Doppler. The operator needs to adjust both probe position and depth to obtain a Doppler signal, noting that these are blind systems where the exact depth and location of the vessel is unknown. Pulsed wave Doppler suffers from aliasing, so could not accurately measure high velocity jets in disease. There was limited impact of PW Doppler in cardiac studies; that is until the work by Holen and Hatle using both CW and PW Doppler (see above) [36, 37]. Stand-alone PW Doppler was largely replaced by duplex Doppler in the 1980s. The one area where stand-alone PW Doppler gained clinical acceptance is in transcranial applications; i.e. use in the intra-cerebral circulation. Transcranial Doppler (TCD) was introduced by Aaslid et al. in1982 [66]. TCD has been used for a diagnosis of cerebrovascular disorders such as stroke, vasospasm and subarachnoid haemorrhage and monitoring of cerebral emboli [67,68].

Multi-gate PW Doppler systems were developed in 1974-75 for simultaneous measurement of the Doppler frequencies from several positions across the vessel. This allowed the first ultrasound measurement of the velocity profile in arteries [69-73]. In terms of clinical application the measurement of velocity profile has not, to date, proven to be useful in its own right. However the measurement of velocity profile has contributed to an understanding of haemodynamics in arteries. At the time established techniques for measurement of velocity profile were invasive and typically involved a hot-wire probe, inserted through arterial puncture, where the probe cooling was related to local blood velocity [74]. This method was unsatisfactory in that, apart from its invasive nature, introduction of the probe affected the flow field. The availability of a non-invasive technique which could measure velocity profile was a major advance in haemodynamic measurement.

VI. Ultrasound angiography

When a CW or multi-gate PW Doppler system was combined with a positioning arm it was possible to build up images of blood flow similar to X-ray angiograms. Ultrasound angiography systems were described for CW Doppler by Reid and Spencer in 1972 [75], for PW Doppler by Hokanson et al. in 1971 [76], and for multi-gate PW Doppler by Mozersky et al. in 1971 [77] and Fish in 1972 [78]. These provide bistable images related to the presence or absence of flow. Curry and White in 1978 [80] developed an ultrasound angiography system in which the image is colour coded dependent on Doppler frequency shift (Fig. 9).

The system developed by Fish [78,79] was further developed by GEC Medical Equipment Ltd (London, UK), later part of Picker International, as the ‘Mobile Artery Visualisation and Imaging System’ or ‘MAVIS’. The device had 30 range gates with a minimum gate separation of 0.64 mm. The device could display 2D images of flow along with the velocity profiles and volumetric flow waveforms (obtained by integration of velocities). Clinical studies were conducted using MAVIS into the 1990s [81-87]. However MAVIS was somewhat ahead of its time; and GEC concluded that ‘the complexity of the equipment and its relatively high cost made it uncompetitive in the ultrasound market’ [88].

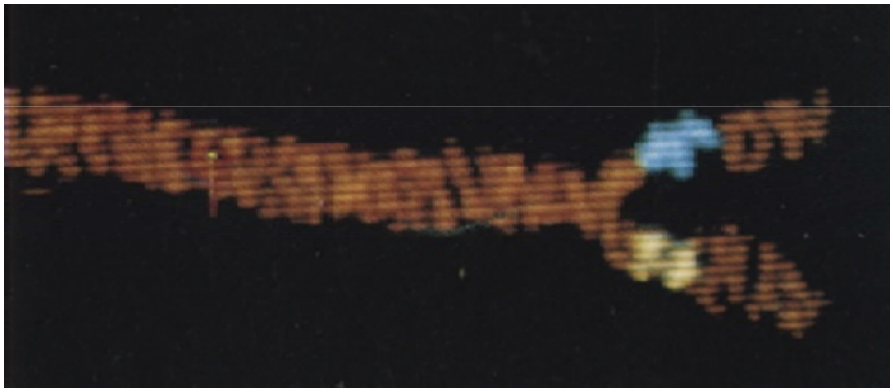

Fig. 9. Scan of the carotid artery using the Echoflow system. The display is colour-coded with higher Doppler frequencies from diseased regions shown in yellow and blue. Reproduced from Ultrasound Med Biol, Vol. no. 4, Curry GR and White DN, Color coded ultrasonic differential velocity arterial scanner (Echoflow), pp. 27-35, copyright Elsevier (1978).

VII. DUPLEX DOPPLER

'Duplex Doppler' refers to the combination of B-mode imaging and Doppler (either CW or PW). Most of the literature below refers to PW duplex Doppler, however CW duplex Doppler has also been reported [89]. Continuous wave duplex continues to be used clinically, particularly in cardiac Doppler to measure high velocities which are subject to aliasing when PW Doppler is used.

The term 'duplex Doppler' was initially introduced by Barber et al in 1974 [90,91] who combined a mechanical sector scanner with an adjacent off-set PW Doppler transducer. This allowed acquisition of real-time B-mode images and real-time Doppler, but not simultaneously. The duplex scanner allowed the operator to identify the vessel of interest, position the sample volume at an exact position within the vessel, freeze the B-mode image and obtain the Doppler waveforms.

The Seattle group continued to develop their duplex system. The review by Beach in 2005 [43] notes that the initial Barber duplex system 'proved too cumbersome to operate', and that the third iteration of the duplex system developed in 1977 had a 'scanhead that could be easily handled'[92,93] (Fig. 10). The Duplex Scanner 3 incorporated a prototype real-time spectrum analyser (Honeywell). Thus the modern duplex system had arrived fully formed, almost.

The company Advanced Technologies Limited (ATL) was established by Baker, as a spin-out from the Seattle group, in 1969. The first commercial duplex system was available in 1974-75. The Mark V Duplex scanner produced by ATL was released in 1980 and used 3 fixed-focus 5 MHz transducers within a rotating wheel (a configuration also called a 'spinner'), described by Breslau in 1982 [94]. During Doppler acquisition the B-mode image was frozen, and one of the transducers was used to generate the Doppler beam (rather than the offset Doppler of previous versions of the system).

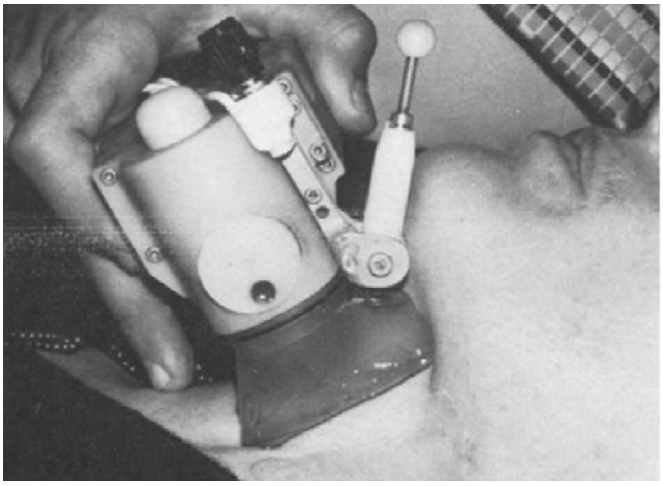

Fig. 10. 'Duplex III' transducer developed by Philips et al (1980). The offset Doppler probe is seen on the right of the transducer. Reproduced from Ultrasound Med Biol, Vol. no. 6; Phillips DJ, Powers JE, Eyer MK, Blackshear Jr WM, Bodily KC, Strandness Jr DE, Baker DW; Detection of peripheral vascular disease using the Duplex scanner III, pp. 205-218, copyright Elsevier (1980).

Contemporaneously SRI International (Menlo Park, California, USA) in partnership with the Mayo Foundation in Rochester (USA) developed their 'B-scan / Doppler' device [73,95]. This consisted of a mechanical sector scanner (reciprocating transducer) with an offset PW Doppler with 20 gates. An improved device consisted of a multi-element annular array with an offset PW Doppler [96].

Using early duplex Doppler studies were undertaken on carotid disease. Diagnostic criteria were established based on the spectral Doppler waveforms [97-101].

In the duplex devices described above, simultaneous real-time display of B-mode and PW Doppler is not possible due to the noise generated from the moving transducers. Typical operation involved a Doppler spectral trace with periodic gaps during which time the B-mode image was updated. Real-time B-mode and PW Doppler requires linear or phased array technology. The group from Osaka (Japan) reported cardiac use of a phased array duplex device consisting of an Aloka SSD-120 B-mode imaging system with an offset Hitachi EUD-4Z PW Doppler [102,103]. The same group reported use of one of the first commercial array duplex systems (Toshiba SSH 11A B-mode incorporating SDS 10A PW Doppler) for which the Doppler beam originated from the array [104-106].

Linear array duplex systems for use in obstetrics were described by Eik-Nes et al. in 1982 [107] and Teague et al in 1985 [108]. These were hybrid systems consisting of a real-time B-mode imaging system and an offset PW Doppler system. Toshiba in 1982 produced one of the first duplex linear arrays incorporating PW Doppler into the array (SSL-53M linear array with the SD-10 pulsed Doppler module). Berson et al. in 1987 [109] described a duplex system which incorporated Doppler into the linear array.

The essential features of the duplex system, incorporating real time B-mode, real time PW Doppler and real-time display of the Doppler spectrum have remained unchanged to the present day (2020).

Applications in areas of the body consisting of multiple vessels with similar waveforms were impossible for stand-alone Doppler. These areas were now accessible using duplex scanning, and the first investigations in the fetus [110] and abdomen [111] followed.

It is worth noting that there were only a few years (4-6) between the development of PW Doppler and the development of duplex ultrasound. Very little of the PW Doppler technology from the intervening period survived into clinical practice, emphasising the importance of the development of duplex ultrasound.

VIII. Colour imaging of blood flow and tissue motion

Despite the very considerable developments and technical adventures in Doppler ultrasound since its introduction in 1959 by Satomura, there was actually little clinical penetration by the early 1980s. The introduction of colour flow, initially by Aloka in 1982, moved Doppler ultrasound into mainstream clinical usage. Colour-flow for the first time provided a real-time view of blood flow which could compliment real time B-mode imaging.

The Seattle group continuing the development of the Duplex system produced the 'Duplex scanner IV', with 3 rotating transducers for formation of the B-mode image and an offset PW Doppler. Brandestini et al in 1978 [112] had developed multi-gate PW Doppler, which was incorporated into the Duplex scanner IV by Eyer et al. in 1981 [113], Fig. 11. By scanning the PW Doppler through the field of view the first colour flow images were obtained. Each image involved manual movement of the PW Doppler transducer over about 20 seconds. The system could also be used in M-mode.

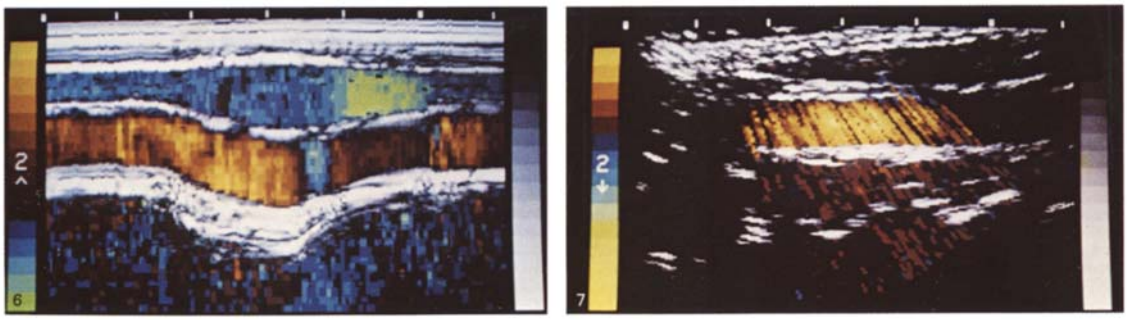

Fig. 11. Colour flow images from Eyer et al. (1981). a) Composite echo/flow M-mode of the jugular vein and common carotid artery during a Valsalva manoeuvre. Increasing time is defined to be from left to right with the entire horizontal axis covering 3.0 seconds. b) B-mode flow map of the common carotid artery obtained in the mid-neck region. Reproduced from Ultrasound Med Biol, Vol. 7; Eyer MK, Brandestini MA, Philips DJ, Baker DW; Color digital echo/Doppler image presentation, pp. 21-31, copyright Elsevier (1981).

The move to real-time colour flow was made possible by the development of the autocorrelation technique for direct measurement of the mean Doppler frequency by Kasai, Namekawa and colleagues from Aloka Company Ltd., Japan [114-116]. In 1982 the first commercial colour flow system was based on the autocorrelator and was produced by Aloka. The autocorrelator requires a minimum of 3 ultrasound pulses to produce a value for estimated mean Doppler frequency (compared to 50-100 for spectral Doppler) and was the breakthrough which made possible real-time colour flow imaging. Colour flow was quickly adopted for cardiac use [117-119] with early studies in arteries [120,121].

Developments in signal processing of colour flow systems are covered by reviews by Evans [49,122,123]. This article will discuss only a small number of relevant developments. The original autocorrelator technique described by Kasai was extended by Loupas et al. in 1995 [124,125], who developed '2D autocorrelation' which has been widely adopted in the commercial sector. The clutter filter is a key component of the processing chain. Early colour flow systems had poor ability to visualise low velocities as a result of the simple design of the clutter filter, and the main use of colour flow was in cardiology where jet velocity is high. Improvements in clutter filter design led to an improvement in the ability of colour flow to visualise lower velocities, and this was followed by widespread clinical adoption of colour flow in radiology.

Three quantities are calculated in colour flow; mean Doppler frequency, Doppler signal power and 'variance'. The variance is a measure of the spread of Doppler frequencies within the received signal. Variance increases in turbulence and may be shown together with the mean-frequency in a composite display.

Display of the Doppler power was a feature of early colour flow systems, but the same settings were used as for display of mean frequency [126-128]. Optimisation of the colour flow settings by Rubin et al. [129,130] enabled improved visualisation of small vessels, and 'power Doppler' became of clinical interest. Power Doppler has been widely used to provide qualitative and quantitative data on vascularity.

Optimisation of the colour system also allows visualisation of tissue motion. The technique of 'Tissue Doppler Imaging' or TDI was introduced by McDicken et al. in 1992 [131]. The signals from tissue are some 40dB higher than from blood so the Doppler gain is reduced. The signal from blood is of very low magnitude so is not displayed. The clutter filter and blood tissue discriminator are redundant. The signal strength is high so fewer pulses are needed to estimate mean Doppler frequency. Tissue Doppler imaging has been widely used in cardiac studies (Fig. 12). From the velocity data the local strain may be estimated which is of interest in detection of ischaemic regions where the strain is reduced [132,133].

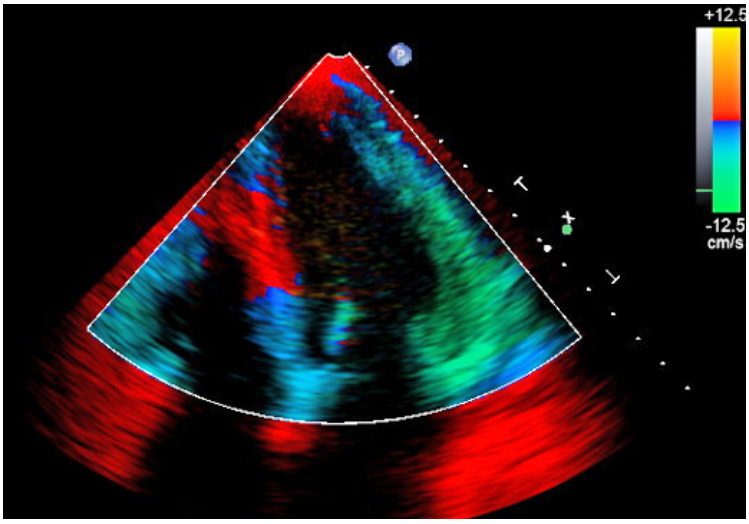

Fig. 12. Doppler tissue image from the heart.

A major limitation of ultrasound imaging, especially colour flow, has been the frame rate which can be achieved. With multiple receive beam-forming [134] frame rates of 200 s^{-1} can be achieved for 2D imaging. This is very high, however achieving high frame rates in 3D imaging and in colour flow is far more challenging using conventional beam-forming techniques. The development of synthetic aperture techniques has led to a vast increase in the amount of data available across all ultrasound imaging modalities. Increase in the information available relies on dispensing with focus-on-transmit. Instead a plane wave or spherical wave is transmitted using all transducer elements, and the image is formed using focus-on-receive. For B-mode imaging frame rates of 10,000 – 20,000 s^{-1} can be generated, with obvious loss of resolution due to the absence of focus-on-transmit. A review of high frame rate techniques for colour flow is provided by Jensen et al. in 2016 [135]. The technique described by Bercoff et al. in 2011 [136] is called 'ultrafast compound Doppler' (UCD) and involves transmission and reception of a series of N plane waves at different angles. Bercoff shows that the frame rate for UCD was 7 times higher than for conventional colour flow, with similar image quality. The availability of such a large amount of data means that choices can be made as to which aspect of image quality to improve. Depending on the application there can be a factor of around 10 increase in frame rate, sensitivity, minimum detectable velocity or minimum detectable vessel diameter. For microvascular imaging, improvements in clutter filtering [137] reduced the minimum detectable velocity from 5 $mm.s^{-1}$ (conventional colour flow) to 0.5 $mm.s^{-1}$, and hence visualisation of vessels down to about 50 micron. New clinical applications have arisen from these developments, in particular 'functional ultrasound' (mirroring functional MRI), concerned with measuring changes in brain activity which are associated with changes in blood flow [138,139].

Colour flow has become an essential feature of the modern cardiovascular ultrasound system. Most clinical practice still relies on spectral Doppler for quantification of blood velocity (see below), with colour flow reserved for qualitative visualisation of the flow-field and of vascularity. While Tissue Doppler Imaging has proven popular in research it has had limited impact on clinical practice. The impact of high frame rate techniques on Doppler ultrasound is still rolling out and it is likely that clinical practice will make more quantitative use of data from colour flow in future.

IX. Measurement of blood velocity and related quantities

A. Estimation of blood velocity

Measurement of blood velocity requires knowledge of the angle between the direction of motion and the Doppler beam. For a single Doppler beam in which the transmit and receive Doppler beams are aligned the velocity may be found by rearranging equation 4:

$$v = \frac{c}{2f}\frac{f_d}{\cos\theta} \quad (10)$$

The ultrasound machine knows the speed of sound and transmit frequency; estimation of velocity therefore requires knowledge of the Doppler frequency shift and the angle θ in the subject.

Early attempts (1970-73) to estimate θ were made using CW and PW Doppler systems. Cumbersome techniques involved finding the orientation of the transducer which is at 90º to the vessel (at which point there is positive and negative symmetry of flow), and then orientating the transducer by a known angle (see page 200 of the text by Evans et al. [49]). The use of 2 or more receive transducers provides an automated method for estimating angle. The velocity component in 2 or more directions is estimated allowing the angle to be calculated [140-143]. These were the forerunner of vector-Doppler techniques described in the next section.

The advent of duplex Doppler provided a clinically-useful means for estimating θ, by enabling the operator to align the angle cursor with the vessel wall. The review on velocity measurement described here relates mostly to clinical ultrasound systems; i.e. those with a single Doppler gate using spectral Doppler.

In clinical use criteria were introduced based on measurement of blood velocity, especially for grading of the degree of stenosis, where the blood velocity increases with degree of stenosis [144]. Typically the maximum Doppler frequency shift has been used (rather than mean frequency), as this is relatively invariant with minor changes in transducer alignment and sample volume position within the vessel.

There was a growing understanding of the Doppler measurement process and the causes of velocity measurement errors following the introduction of the duplex scanner in the 1970s. Implicit within the Doppler equation is the assumption that a single velocity will give rise to a single Doppler frequency shift. In fact a single velocity will give rise to a range of Doppler frequencies; a phenomenon called 'spectral broadening'. Newhouse et al. in 1977 [145] demonstrated that the finite width of the transducer gives rise to broadening as a result of the range of angles which the blood velocity subtends at the transducer. It was shown by Censor in 1988 [146] that the 'geometric spectral broadening' f_{gsb} is given by:

$$f_{gsb} = \left(\frac{2fv}{c}\right)\left(\frac{D\sin\theta}{2L}\right) \quad (11)$$

where D is the width of the Doppler aperture and L is the depth of the Doppler sample volume.

Newhouse et al. in 1976 [147] investigated transit time broadening which is due to the finite time taken for scatterers to cross the beam, then proposed that transit time and geometric spectral broadening were the same phenomenon [148]. This equivalence was accepted for many years before Guidi et al. in 2000 [149] demonstrated that these were different phenomena, however this had actually been proven 14 years previously by Fish in 1986 [150], equation 11.81, p363). The data from Guidi suggest that, around the transducer focus, spectral broadening is dominated by the geometric component (a factor of 6 compared to transit time broadening).

When linear arrays are used to generate the Doppler beam this leads to a large amount of geometric spectral broadening, which in turn leads to overestimation of blood velocity [151,152]. The explanation is that the ultrasound machine angle-corrects to the middle of the array, whereas the highest Doppler frequencies are found at the edge of the array. In fact the equation which is relevant for the highest Doppler frequency shift f_{max} is a combination of equation 4 and 11 [153]:

$$f_{max} = \left(\frac{2fv}{c}\right)\left(\cos\vartheta + \frac{D}{2L}\sin\theta\right) \quad (12)$$

The error in estimated maximum velocity varies with angle, depth and machine. Typical errors are in the range 0-40% for clinical settings and potentially lead to impact on selection of patients for surgery [154]. Despite the known errors there has been no move on the part of manufacturers to provide correct estimation of blood velocity.

B. Estimation of pressure gradient

A method for estimation of pressure gradient across cardiac valves was reported by Holen and then by Hatle [38-41]. The method is based on a consideration of the Bernoulli equation which concerns energy in flow. The pressure drop is:

$$P_1 - P_2 = \frac{1}{2}\rho({v_2}^2 - {v_1}^2) + \rho\int_1^2 \frac{dv}{dt}ds + R(v) \quad (13)$$

where suffix 1 denotes the fluid position element in front of the valve and suffix 2 in the valve jet; P is the pressure, v is the velocity vector of the fluid element, and ds is the path element.

The first term relates to change in kinetic energy, the second term represents acceleration caused by change in velocity with time, and the third term represents viscous loss.

Holen and Hatle argued that the second and third terms were small compared to the first term. Noting also that $v_2 >> v_1$, a simplified equation results:

$$P_1 - P_2 = \frac{1}{2}\rho{v_2}^2 \quad (14)$$

Inserting the value for density, and expressing the pressure difference in mm Hg, the final equation is derived:

$$P_1 - P_2 = 4{v_2}^2 \quad (15)$$

This technique has had widespread clinical adoption, initially using stand-alone CW/PW Doppler systems, then with duplex Doppler.

C. Estimation of volumetric flow

The first attempts to measure volumetric flow were undertaken using multi-gate PW Doppler systems in 1974-75 [69-73]. These systems did not incorporate B-mode imaging so the procedures described in subsection A were used to measure the beam-vessel angle. Assuming that flow was axial (non-rotational) and axially symmetric, the velocity profile could be integrated to produce an estimate of the instantaneous volumetric flow. The mean volumetric flow could then be obtained by integration over the cardiac cycle.

Volumetric flow Q was estimated using a duplex scanner with measurement of diameter d from the B-mode image (from which area is calculated assuming that the vessel is circular) and measurement of the velocity waveform from the Doppler spectral data, noting that this has been angle-corrected by alignment of the angle cursor with the vessel wall:

$$Q = V_{ta}\frac{\pi d^2}{4} \quad (16)$$

where V_{ta} is the time-averaged velocity obtained from the Doppler waveforms.

Early reports of volumetric flow measured using duplex Doppler were published from 1979-1985 [110,155-157]. While the equation used to estimate volumetric flow is straightforward, there are several sources of error which must be considered. The principle problem is the relationship between the Doppler statistic and the mean velocity. Commonly the mean Doppler frequency is used, and it is assumed that the mean frequency when angle corrected is equal to the instantaneous mean velocity. This might be the case were the vessel uniformly insonated. However a typical Doppler beam is thin compared to the vessel diameter so that the mean velocity calculated from mean frequency is usually overestimated; for example for a very thin beam in steady flow the overestimation is 33% [158]. Further complexity arises in pulsatile flow as the velocity profile changes through the cardiac cycle. In addition mean frequency is highly sensitive to small changes in alignment between the vessel and the beam. An extensive discussion of the errors in volumetric flow is provided in by Gill [159], Evans [160] and in chapter 11 of the textbook by Evans et al. [49]. When compared with 'gold standard' measurements it was found the median rms error in flow measurement across several studies was 16% (range 11-34%) [58]. The mean Doppler frequency has remained the statistic of choice in the literature, despite the known problems and errors.

An alternative approach is to use the maximum Doppler frequency, noting that the overestimation of velocity as a result of geometric spectral broadening must be corrected. Maximum frequency has the advantage over mean frequency of not varying for small misalignments of the transducer caused by movement of the operator or patient. The maximum velocity is estimated from the maximum Doppler frequency shift, and there are 2 methods which have been developed which allow estimation of flow from maximum velocity. For estimation of time-averaged flow rate it can be assumed that the average velocity profile is parabolic, provided that flow is fully-developed [161]. In this case the time-average maximum velocity $V_{ta\text{-}max}$ is estimated and flow Q can be calculated:

$$Q = \frac{V_{ta-max}}{2}\frac{\pi d^2}{4} \quad (17)$$

The second method for estimation of volumetric flow from the maximum velocity waveform makes use of the Womersley equations [162]. These equations describe the velocity profiles during fully-developed flow for a Newtonian fluid. The equations are formulated in terms of diameter and flow rate, however these can be modified to allow input of the diameter and the centre-line (maximum velocity) waveform [163] with output of the time-varying velocity profile data. Once the time-varying velocity profile data is available, volumetric flow can be obtained by integration of the profile data, and in addition this technique also gives the time-varying wall shear rate [164] (Fig. 13).

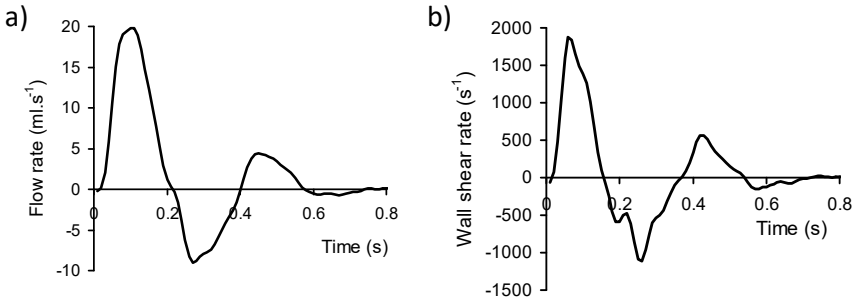

Fig. 13. Estimation of volumetric flow and wall shear stress (Blake et al. 2008 [164]).

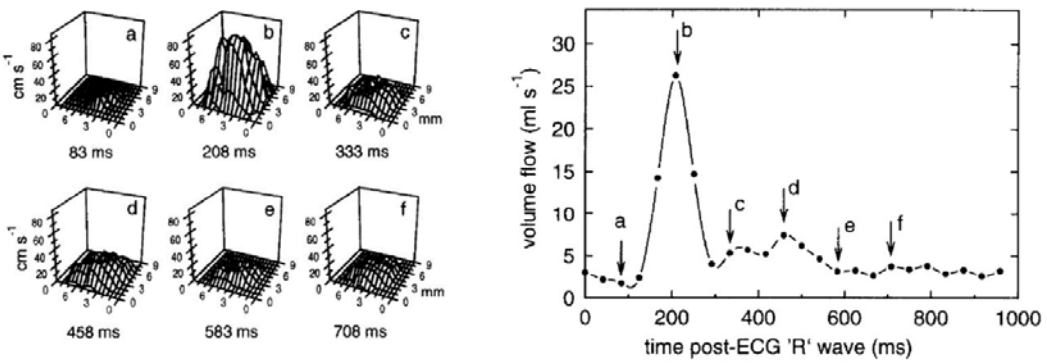

Fig. 14. Estimation of 2D velocity profile and flow. Reproduced from Ultrasound Med Biol, Vol. 21; Picot PA, Fruitman M, Rankin RN, Fenster A; Rapid volume flow rate estimation using transverse colour Doppler Imaging, pp. 1199-1209, copyright Elsevier (1995).

Colour flow provides multi-gate velocity information and has been used to provide estimation of volumetric flow. This has been used to measure the 1D velocity profile, from which volumetric flow has been calculated assuming axially symmetric fully-developed flow [165]. Colour flow has also been used to estimate volumetric flow from the 2D velocity profile using an oblique cross section through the vessel [166], Figure 14.

The discussion of this section has emphasised the difficulties and assumptions in estimation of volumetric flow using the duplex system. Ideally what is required is a method which does not make assumptions related to fully-developed flow or axial symmetry. It is likely that the techniques, discussed in the next section, which are able to measure 3D and 3-component velocity field data are likely to provide accurate and clinically useful information on flow rate and other haemodynamic quantities.

X. 3D AND VECTOR DOPPLER

This section will cover 3D and vector Doppler. These are deliberately combined in that they are attempting to solve the same problem which is a more complete characterisation of the flow field. Early studies, described above, on velocity measurement largely assumed that the blood is flowing parallel to the vessel wall; this assumption is embedded in the phrase 'beam-vessel angle' to describe the angle between the beam and the direction of motion. Understanding of haemodynamics gained momentum in the 1980s and 1990s due to the availability of tools which could measure flow patterns. In the lab optically transparent phantoms were developed where complex flow patterns could be seen in a carotid model [167]. The first numerical simulations were undertaken of blood flow by Perktold et al in 1984 [168] and Friedman and Ehrlich in 1984 [169]. Both ultrasound and MRI were used to demonstrate spiral flow in arteries [170-172]. A key concept is the idea of 'fully developed flow'. This can be understood with reference to flow from a reservoir into a long straight pipe. Near the entrance to the pipe the velocity profile is flat and after a certain distance called the 'inlet length' the velocity profile settles down to a fixed shape (for Newtonian flow this is a parabola). Any change of geometry such as a bend, bifurcation or disease will cause alterations in velocity profile. The underlying assumption of much of the discussion on velocity measurement in section IX is that the flow is fully-developed. In some arteries in health flow may well be fully-developed, for example in the distal regions of arteries in the arm and leg. However many arteries are short with strong curvature and flow will not be fully developed. In addition there are helical components to flow. There is helical flow in the normal aorta [173] and bending of arteries and bifurcations will induce helical flow [174]. Disease such as atherosclerosis and aneurysms will also affect flow profiles and can cause non-axial flow. The common carotid artery has been the subject of considerable interest in ultrasound. Figure 15 is an image of streamlines of flow calculated using computational fluid dynamics showing highly complex flow patterns. A full characterisation of flow requires 3 spatial components, 3 velocity components and time, so 7 components in all. Full time-varying flow field data is sometimes referred to as '7D flow'. It will be seen that the history of Doppler ultrasound is one of progression towards 7D flow.

Early work on 3D Doppler involved mechanically scanning the array [172]. A series of transverse images were acquired while moving the transducer along the length of the artery. There is change in diameter of the artery during the cardiac cycle, so ECG gating was necessary in order to collect data at the same point in the cycle. Colour flow images were acquired which made one of the first observations of helical flow in the carotid artery (Fig. 16). The development of 3D ultrasound is described in the review by Fenster in 2011 [175]. Early commercial 3D systems used a swept linear array. The first 3D ultrasound system based on a 2D array was developed by Volumetrics Medical Imaging (Durham, North Carolina, USA) and available at the end of 1990s (Fig. 17). The Volumetrics system was based on technology developed by the group at Duke University [176]. Later Philips Medical Systems produced a 2D array system with part of the beam-forming within the transducer. In 2020 commercial 3D ultrasound systems are a mix of swept array, 2D array, and (for endoprobe systems) mechanical pullback.

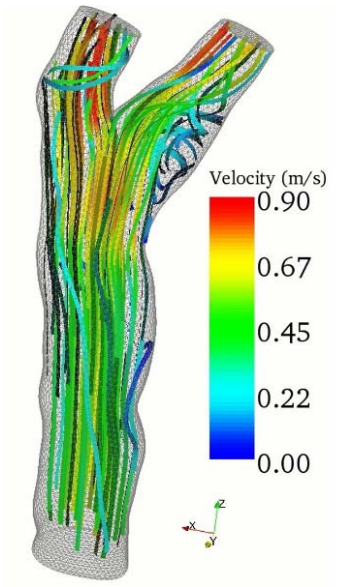

Fig. 15. Streamlines of flow in a diseased carotid artery; showing helical flow and recirculation in the bulb.

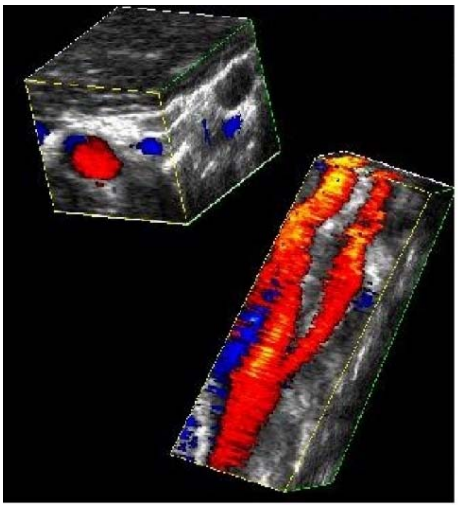

Fig. 16. 3D colour flow images of the carotid artery. From Aaron Fenster, London, Ontario.

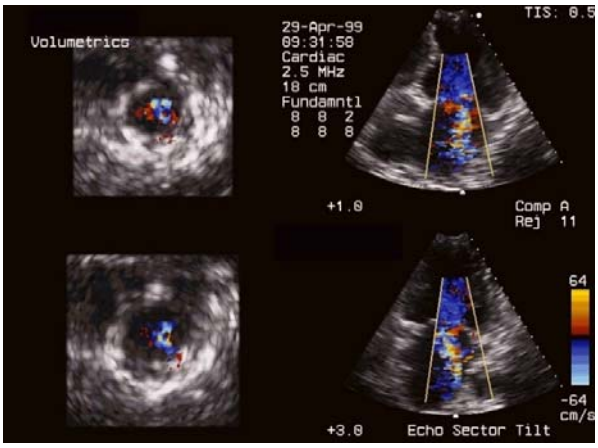

Fig. 17. 3D colour flow imaging using the Volumetrics system from 1999.

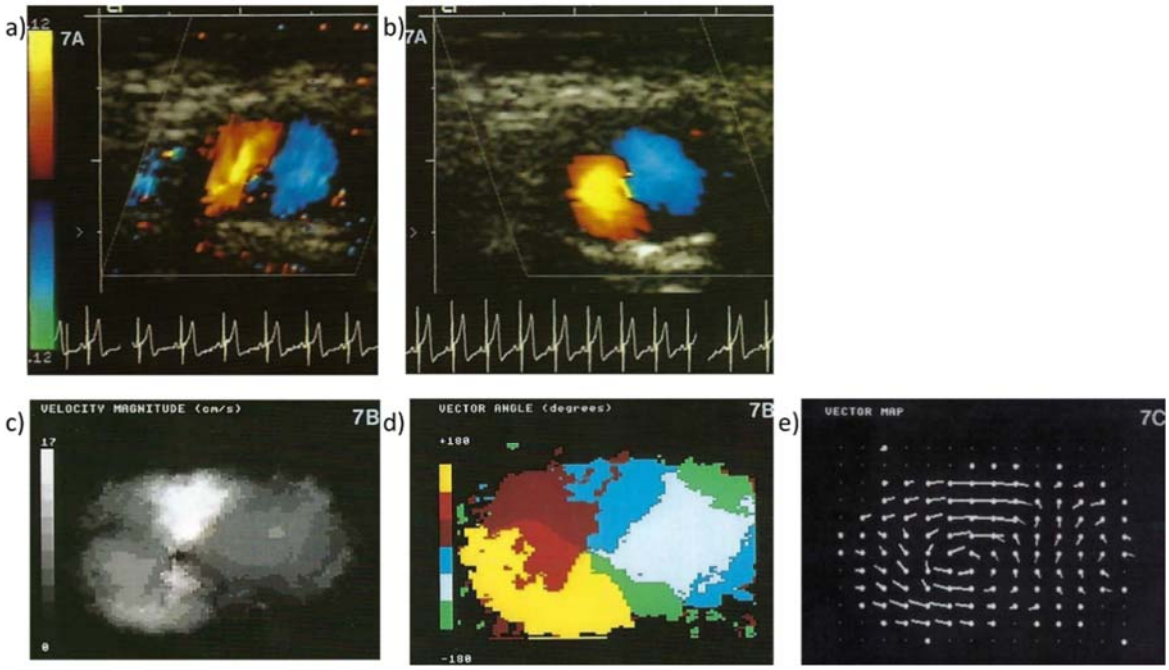

Fig. 18. Vector Doppler images showing spiral flow in the femoral artery. a) and b) colour flow images obtained with the beam pointed to the left then right, c) velocity magnitude, d) vector angle, e) vector display. From Hoskins PR, Fleming A, Stonebridge P, Allan PL, Cameron D. Scan-plane vector maps and secondary flow motions. European Journal of Ultrasound 1994;1:159-169.

Single-beam Doppler systems provide information on 1 velocity component; the component aligned with the ultrasound beam. Vector Doppler involves estimation of velocity components from different directions and compounding these to obtain the velocity magnitude and direction. Vector Doppler systems based on single element transducers were able to make measurements from a single sample volume of 2 velocity components [177-180] or 3 components [178-184]. 2D vector Doppler images may be obtained by using colour flow, with the colour beam steered in 2 different directions [172,185-189]; Fig. 18.

In addition it is possible to use the spectral width to estimate the direction of motion. Combining equations 4 and 11 gives the fractional spectral width:

$$\frac{f_{sw}}{f_{mean}} = \frac{D \tan\theta}{L} \tag{18}$$

where f_{mean} is the mean Doppler frequency, and f_{sw} is the spectral width. Rearranging equation 11 gives:

$$\theta = \tan^{-1}\left(\frac{L}{D}\frac{f_{sw}}{f_{mean}}\right) \tag{19}$$

Equation 12 allows the angle θ to be estimated using a single beam, provided that it is only geometric spectral broadening that is contributing to the spectral broadening. This method has been used to estimate 2 components using a single beam system and 3 components in a 2-beam system [181,182].

A patent was published by Hall et al. in 1995 [190] for an array vector Doppler system in which the array was divided into a central transmit aperture with receive apertures on either side. A prototype array based vector Doppler system was produced by ATL Ultrasound using a similar approach, which proved successful in phantoms and in normal volunteers in acquiring velocity measurements which were angle-independent [191,192]. However despite the ease with which vector Doppler could be adopted on array based systems, there was no commercial adoption of cross-beam vector Doppler and hence no clinical penetration. A review of cross-beam vector Doppler is provided by Dunmire et al. in 2000 [193].

The first commercial colour vector Doppler system was available from BK Medical using the transverse oscillation (TO) method [194,195]. This method creates an oscillation in the transverse direction from which the transverse velocity component can be estimated. Creation of the transverse oscillation is performed in reception; this produces 2 beams from which the transverse velocity component can be estimated. The transmit beam is unchanged in TO from conventional Doppler, so that TO has a higher frame rate and larger field of view than comparable cross-beam techniques.

The TO method has been modified for 3 component velocity estimation [196,197] with 2D 3-component velocity profiles obtained from carotid arteries [198]. The same methodology was also used to acquire 3D 3-component flow in the heart using ECG gating at 50 frames per second [199].

The techniques above, involving cross-beam and transverse oscillation provide real-time 2D imaging with 2 velocity components, so 5 of the 7 dimensions. As noted above recent years have seen the development of high frame rate synthetic aperture techniques involving either plane wave insonation or spherical wave insonation, with focus on receive. Frame rates of over 3000 s^{-1} were achieved for real-time 2D 3-component imaging of flow in the carotid artery [200]. It is using synthetic aperture imaging that real-time 3D 3-component (i.e. 7D) flow imaging is likely to become available in the near future. Further details of recent developments in vector Doppler are available in the reviews by Jensen et al. [135,201].

XI. Chronological summary of major developments by decade

1950s

CW Doppler systems developed by Satomura (Osaka, Japan) for measurement of heart wall motion and blood flow.
Commercial Doppler system; the Ultrasonic Blood Rheograph (Nippon Electric Company).
Invasive Doppler probes developed by Franklin (Seattle, USA).

1960s

Development of CW Doppler technology; flow discrimination methods, real-time single-line display of mean Doppler frequency from a zero-crossing detector, off-line spectral display.
PW Doppler systems.

1970s

Multi-gate Doppler systems, allowing measurement of velocity profile.
Ultrasound angiography.
Duplex Doppler.
Colour flow system using slow-sweep of Doppler beam.
Methods for angle-estimation (based on multiple single elements).
Identification of causes of spectral broadening; geometric and transit time.
Formulation of RI and PI for waveform analysis.
Methods for estimation of pressure gradient across cardiac valves from Doppler measurements of velocity.
Volumetric flow estimation using duplex scanners.

1980s

Real-time colour flow system with applications in the heart, and later in vessels.
Theoretical understanding of the origin of Doppler spectra.
Doppler waveform analysis; quantification of waveform shape and spectral content for use in diagnosis.
Vector Doppler systems (based on multiple single elements).

1990s

Tissue Doppler Imaging (of heart motion, and later vessel wall motion).
Power Doppler.
Colour vector Doppler (off-line then later real-time).
3D colour-flow.
Improved understanding of the estimation of blood velocity and related quantities using Doppler.

2000-2020

High frame rate Doppler and related applications (colour flow, spectral Doppler, vector Doppler, microvascular imaging, functional ultrasound).

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