**Stein Olav Samstad** 

# CROSS SECTIONAL FLOW VELOCITY PROFILES FROM TWO-DIMENSIONAL DOPPLER ULTRASOUND

Studies on early mitral blood flow



University of Trondheim Department of Medicine Trondheim - Norway



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## Contents

| Page |
|------|
| 4    |
| 6    |
| 7    |
| 10   |
| 11   |
| 11   |
| 19   |
| 22   |
| 27   |
| 28   |
| 37   |
|      |

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### List of papers

I Samstad S O, Torp H G, Linker D T, Rossvoll O, Skjaerpe T, Johansen E, Kristoffersen K, Angelsen B A J, Hatle L.
 Cross sectional early mitral flow velocity profiles from colour Doppler.

British Heart Journal 1989; 62: 177 - 84

 II Samstad S O, Torp H G, Matre K, Rossvoll O, Segadal L, Piene H.
 Instantaneous cross-sectional flow velocity profiles: A comparative study of two ultrasound Doppler methods applied to an in vitro pulsatile flow model.

Journal of the American Society of Echocardiography 1990; 3: 451 - 464

III Samstad S O, Bathen J, Rossvoll O, Torp H G, Skjaerpe T, Hatle L. Impact of changes in heart rate and stroke volume on the cross sectional flow velocity distribution of diastolic mitral blood flow: a study on 6 patients with pacemakers programmed at different heart rates.

International Journal of Cardiac Imaging 1992; 8: 75 - 83

IV Samstad S O, Rossvoll O, Torp H G, Skjaerpe T, Hatle L.
 Cross sectional early mitral flow velocity profiles from color Doppler in patients with mitral valve disease.

Circulation 1992; 86; 748 - 55

V Samstad S O, Rossvoll O, Torp H G, Skjaerpe T, Hatle L.
 Interobserver and intraobserver variation of cross sectional early mitral flow velocity profiles from color Doppler.

Journal of Cardiovascular Diagnosis and Procedures 1993; 11: 167 - 78

The papers will later be referred to by their Roman numbers.

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### Introduction

Volume flow estimates became a quantitative measurement of cardiac performance with the introduction of cardiac catheterisation, and combined with pressure measurements the severity of valvular regurgitations, stenoses and shunts could be quantified <sup>1</sup>. The techniques were widely used, but the invasive nature of the methods made them less than optimal for the follow-up of patients. Thus, a need for noninvasive investigative tools for quantitative measurements of cardiac performance was apparent.

The first attempts to obtain information on heart structures and function with a technique based on ultrasound echocardiography, were reported by Edler in 1954<sup>2</sup>. The first use of pulsed wave Doppler ultrasound to record blood flow velocities noninvasively in clinical cardiology, was reported in 1972 when atrial septal defects were diagnosed by the flow velocity patterns in the jugular vein<sup>3</sup>. In 1973 a study on the localisation of cardiac murmurs was published<sup>4</sup>. With continuous wave Doppler ultrasound, Holen and coworkers in 1976 were able to quantify jet velocities<sup>5</sup>. They also established the relationship between jet velocities and pressure drop. Later, Hatle and coworkers introduced the "modified" Bernoulli equation to calculate pressure drops across stenotic orifices<sup>6</sup>.

Several methods for cardiac output measurements by use of echocardiography alone <sup>7-9</sup>, or by combining Doppler recordings of blood flow velocities with flow area measurements with echocardiography, were published <sup>10-16</sup>. Methods using the continuity equation of mass transportation were developed to calculate the valve orifice area in aortic stenosis <sup>17, 18</sup> as well as estimates of regurgitation fraction in mitral or aortic valvular incompetence <sup>19-22</sup>. When aortic regurgitation is present, cardiac output cannot be estimated from recordings made in the aortic orifice, and other sites have been used <sup>13-16, 23-27</sup>.

Although popular, some disadvantages of the methods that were developed for volume flow calculations are apparent. The exact measurement of the instantaneous blood flow area with M-mode or two-dimensional echocardiography may be difficult, especially at the mitral valve <sup>28-29</sup>. Furthermore, pulsed Doppler ultrasound gives velocity information from only a minor part of the actual flow area

in normal valves. Thus the flow velocity recordings from pulsed Doppler could lead to misinterpretation since they may not be representative for the whole flow area <sup>30</sup>.

Laminar and steady flow through straight tubes has a parabolic cross sectional flow velocity distribution. At the inlet, and during flow acceleration, the flow profile tends to be flattened <sup>31</sup>. In the heart and great vessels where the anatomy deviates from these conditions, the flow velocity distribution becomes complex and only a few attempts to describe such flow velocity patterns from numerical analyses have been made <sup>32, 33</sup>.

Both noninvasive and invasive methods have been used to describe the cross sectional flow velocity distribution at various sites in the heart and great vessels. For flow through the mitral orifice only one study, based on the Pitot principle, has been published <sup>34</sup>. This principle is an indirect method of flow velocity recording based on measurements of pressure differences between two transducers located at the same position with one directed upstream and the other downstream. This invasive method was used in a study on canine mitral blood flow by Taylor and Whammond <sup>34</sup>.

For the study of the cross sectional flow velocity profiles in the aorta, the aortic orifice and the left ventricular outflow tract, various methods have been used. Seed and Wood used a hot-film anemometer to characterize blood flow velocity distribution in the proximal aorta in dogs <sup>35</sup>. Paulsen and Hasenkam used the same method to obtain three-dimensional visualization of velocity profiles in the ascending aorta in dogs, and later the method was applied to the human ascending aorta by the same investigators <sup>36, 37</sup>.

Another invasive approach was published by Lucas and coworkers who used an intraluminar probe with pulsed Doppler ultrasound recordings from the ascending aorta in dogs <sup>38</sup>. With the same method Segadal and Matre studied blood flow velocity distribution in the ascending aorta in patients undergoing cardiac surgery <sup>39</sup>.

Magnetic resonance imaging has been used to describe the flow velocity patterns in the human ascending and descending aorta <sup>40, 41</sup>.

A non-invasive approach to the characterisation of cross sectional flow velocity distribution in the human ascending aorta was published by Jenni and coworkers using a multigate pulsed Doppler instrument <sup>42</sup>.

After the introduction of two-dimensional color flow mapping with Doppler ultrasound, Miyatake and coworkers used the method to describe the right atrial flow velocity distribution during the cardiac cycle <sup>43</sup>. This study was based on visual impression of the flow velocity distribution without quantitative measurements.

Sahn and coworkers described a method for quantitative flow velocity measurements from color Doppler ultrasound recordings by decoding video recordings of color flow maps <sup>44</sup>. This method has later been used in experimental in vitro studies on the flow velocity distribution proximal and distal to various stenotic orifices <sup>45</sup>.

Recently two-dimensional digital acquisition of flow velocity data from color Doppler instruments has been used for the study of the flow velocity distribution in the aortic annulus and the left ventricular outflow tract <sup>46-48</sup>. Based on the method in the present study these authors used time interpolation between the velocity data from sequentially recorded flow maps to compensate for the distortion of the flow velocity profiles introduced by the color Doppler technique.

### Aims of the study

With the development of the Doppler and the echocardiographic ultrasound technique a non-invasive approach to quantitative measurements of blood flow became available. In non-stenotic valves, flow velocity recordings were usually made from only a limited part of the total flow area, and some of the new methods were hampered by the lack of knowledge of whether the measurements were representative for the flow velocity distribution across the whole flow area or not. This lack of information on the cross sectional flow velocity distribution in the mitral orifice was evident. Because this is essential for volume flow measurements the aims of this study were:

- Development of a new, noninvasive method for the study of instantaneous cross sectional flow velocity profiles in the heart and great vessels, based on Doppler color flow mapping.
- 2. Comparison of the new method with an established method in an in vitro model with pulsatile flow.
- 3. To study the inter- and intraobserver variation of the new method when applied to the early mitral flow.
- Application of the method in patients with varying cardiac stroke volume to study the effect of changes in stroke volume on the cross sectional flow velocity distribution of mitral blood flow.
- 5. Application of the method in patients with mitral valve disease to study the effect of mitral valve stenosis or regurgitation on the cross sectional flow velocity distribution of early mitral blood flow.

### Subjects and patients

In papers I and V normal subjects were examined. Ten subject were included in each study. In paper III 6 patients with atrial fibrillation and complete atrioventricular conduction block, dependent on cardiac pace-makers were studied. In paper IV 10 patients with mitral stenosis and 10 with mitral regurgitation were included. Five of the patients with mitral stenosis also had small (3) or moderate (2) mitral regurgitation. A total of 78 individual recordings from mitral blood flow in 46 subjects / patients were included in the studies. All recordings were done after informed consent and none of the recordings were used in more than one paper.

### Methods

#### Echocardiography and Doppler ultrasound

Echocardiography is based on directed transmission of sound waves in the megahertz frequency band and recording of the backscattered sound waves from the heart and its surrounding tissue. In tissue imaging mode the information from a sector scan on signal intensity of the backscattered ultrasound signals and the time from sound transmission to recording, is converted to tissue images and displayed on a monitor.

To measure blood flow velocities the frequency shift of the backscattered ultrasound waves are used in the Doppler equation:  $v = \frac{cf_d}{2:f_0 \cdot \cos \theta}$  where v is the velocity of the volume element of blood cells, c is the velocity of sound,  $f_d$  is the frequency shift,  $f_0$  is the frequency of the transmitted ultrasound signal and  $\cos \Theta$  is the cosine to the angle between the ultrasonic beam and the velocity vector of the element of blood cells<sup>49</sup>.

The conventional Doppler recordings in papers II and III were based on Doppler spectrum analysis. The spectral curves were traced along the middle part of the dense spectral band surrounding the curves (modal velocities), and the mean velocity was calculated as the area below the digitized curve divided by the flow time. In recordings from laminar blood flow the displayed spectrum is usually narrow-banded in the absence of noise, and a mean velocity estimate can be obtained by tracing the dense part of the spectrum.

With the two-dimensional Doppler method the velocity estimates are done with a technique that automatically calculates the mean velocity from each sample volume along the ultrasound beam <sup>50, 51</sup>. Each velocity estimate is based on an autocorrelation function of the frequency and the intensity of the backscattered ultrasound signal. Compared with conventional pulsed Doppler recordings the two-dimensional Doppler ultrasound technique utilises a lower number of pulses per ultrasound beam in order to obtain an adequate frame rate. The time required to obtain flow velocity data can be varied by excluding part of the velocity spectrum by increasing the high pass filter limit, an increased high pass filter limit gives a shorter sweep-time. The main reason for increasing the high pass filter limit is to suppress tissue signals. Secondly, the frame rate can be varied by changing the time for sampling and analysing the ultrasound velocity data from each sample volume. A side-effect of shortening the sweep time is sample points with no velocity information. To overcome such points of missing velocity data, smoothing of the velocity map in radial direction can be done within the instrument. The use of such smoothing filters on the flow velocity maps implies only a moderate decrease in spatial resolution <sup>52</sup>.

#### Ultrasound equipment

**CFM 700** (VingMed Sound A/S, Oslo, Norway). This instrument was used in all studies to obtain two-dimensional Doppler ultrasound recordings from the mitral blood flow. It is a combined two-dimensional and M-mode tissue imaging ultrasonograph with facilities for pulsed Doppler with low or high pulse repetition frequency, continuous wave Doppler, color M-mode Doppler (color coded multigated Doppler) and color flow mapping.

Various types of annular array mechanical transducers were used. In paper I a combined 3 MHz imaging and Doppler transducer was used and in paper II a combined 7 MHz imaging and 6 MHz Doppler transducer. A combined 3 MHz imaging and 2.5 MHz Doppler transducer was used in papers III, IV and V.



#### Fig.1.

Beam profiles from a 2.5 MHz annular array color Doppler transducer with a radial resolution of approximately 1 mm. Inner trace is at a depth of 7 cm from the transducer, inner middle and outer middle traces from depths of 9 and 11 cm from the transducer and the outer trace is from a depth of 13 cm from the transducer. (Courtesy to Torp, HG, Institute of Biomedical Engineering, University of Trondheim).

The lateral resolution of the Doppler ultrasound beam (fig.1) was defined as a 50 % decrease in backscattered ultrasound signal. In paper I the lateral resolution was 2.1 - 2.5 mm at the depths of blood flow velocity recording, in paper II it was 1.5 mm at a depth ranging from 2.1 to 2.8 cm from the transducer and in papers III, IV and V the lateral resolution was less than 3mm at the depths of recording

The radial resolution depended on the extension of the color flow sector. The radial resolution was calculated by dividing the difference in distance between the distal and proximal extension of the flow sector by the number of sample gates in each ultrasound beam direction. Thus the radial resolution varied with the different depth ranges used, but the radial resolution was better than the lateral resolution in each study. In the color Doppler mode of the instrument the transducer transmits and records multigated ultrasound signals along sequential beams evenly distributed within the flow sector. The flow sector scan consisted of

64 times 64 sample volumes which were color encoded immediately before they were displayed on the monitor of the instrument. In parallel to being color coded, the flow velocity data were passed to a continuously updated play-back memory of the instrument.

The time spent for tissue data sampling was approximately 20 ms whereas the time used for sampling the Doppler ultrasound data varied. In paper I the frame rates varied between recordings. In paper II, two defined frame rates were used with sweep times of 80 and 230 ms respectively, and in paper III the sweep time was either 54 or 65 ms. In papers IV and V a fixed frame rate of 12 frames per second was used with a corresponding sweep time for the Doppler ultrasound sampling of 65 ms.

The high pass filter setting was 21 cm/s in paper I, 8 cm/s in paper II and 19 cm/s in papers III, IV and V, excluding velocities below these values in the flow velocity data. The maximum values for the recordable velocities varied with the transducer frequencies used, with the depth of velocity recording and with the high pass filter setting. With a known blood flow direction the velocity baseline can be shifted and the maximum recordable velocity without aliasing of the pulsed Doppler signal was thus equal to two times the Nyquist frequency minus the high pass filter limit. In paper I this maximum velocity was 120 cm/s and in papers III, IV and V it was 180 cm/s. In paper II this limit was of minor interest since the velocities recorded from the hydromechanical simulator were externally controlled and adjusted to fit the actual ultrasound instruments.

**SD 100** (VingMed Sound A/S, Oslo, Norway). This is a single Doppler ultrasound instrument with pulsed and continuous wave Doppler modalities. In paper II this instrument was connected to a custom made, small transducer mounted on the tip of a needle to record flow velocities within a tube. The transducer frequency was 10 MHz, and the lateral resolution of the ultrasound beam was about 1 mm at the position for velocity recording 3 mm upstream from the probe. In this study the high pass filter limit of the displayed velocity spectrum was set to 4 cm/s.

#### Hydromechanical flow simulator

In paper II a hydromechanical flow simulator was used to produce pulsatile flow in a silicon rubber tube system. The tube system was filled with a blood substitute with approximately the same specific weight as whole blood. Dextran microsphere particles (Sephadex G-25 superfine 100, Pharmacia LKB, Bromma, Sweden) suspended in distiled water was used as ultrasound contrast medium. The blood substitute was propelled through the tube system by a pneumatic pump with a control unit where the duration of driving pressure and the magnitude of the pumping pressure could be modulated to simulate flow velocity patterns in the human aorta <sup>53</sup>.

#### **Recording procedures**

Patients and normal subjects were placed in the recumbent position slightly rotated to the left to obtain an optimum window to the mitral valve from a apical position. In all studies a four chamber view was used.

Recordings were done while the patients held their respiration at end expiration without closing the glottis. This was done to avoid thoracic movement due to respiration and to avoid respiratory changes in the heart rate and in mitral blood flow. The longest periods of held respiration of 25 s occurred in one of the normal subjects in paper I with a heart rate of 41 beats per minute.

In paper II the color flow transducer was attached with calipers with a fixed relative position to the flow tube of the hydromechanical flow simulator whereas the single Doppler probe was moved stepvise along a fixed axis of the holding device.

In papers I, II and III the increase in the time lag from the trigger signal to the initiation of the updating of the tissue and flow maps was adjusted manually between each heart cycle. This was done by step-wise rotating of the controller knob on the ultrasonograph which increased the time lag with 20 ms in each step. In papers IV and V this increase was done automatically by the ultrasonograph. In this way color flow maps, one in each heart cycle, was recorded from the onset of early mitral flow until the end of the diastasis period with cessation of blood flow or the onset of flow due to atrial systole.

#### Data processing

For the purpose of this study the flow velocity data was accessible at three different levels of the instrument. In four of the subjects in paper I the flow velocity data was accessed as raw digital ultrasound Doppler data from the front end of the ultrasonograph by use of a custom made interface, PUDGI (Portable Ultrasound Data Grabber and Interface), connected to a Stride 460 computer (Stride Micro, Reno, NV, USA). In the other six subjects in paper I the flow velocity data were accessed as digital flow velocity data from the replay memory of the ultrasonograph by way of a commercial data port (NBDIO 24, National Instruments, Austin, Texas, USA) and a custom made data program to an IBM-compatible computer.

In papers II,III, IV and V the combined tissue and two-dimensional flow velocity recordings from each series of the sequentially delayed sweeps were transferred from the digital replay memory of the ultrasonograph to an external computer (Macintosh II, Apple Computers, Inc. Cupertino, California, USA) with the use of a commercial data program (TransDisp, VingMed Sound A/S, Oslo, Norway) by way of the same data port as in paper I <sup>54</sup>.

The third level of data access, tape recordings of the displayed tissue and flow data as they appeared on the monitor, was only used to check the triggering function.

Two different types of digitizing tablets were used. In paper II the spectral curves of the recorded velocities with the intraluminal transducer were digitized by hand on a graphic tablet (Tektronix 4957, Tektronix Inc., Beaverton, Oregon, USA) interfaced to a computer (ND-500, Norsk Data, Oslo, Norway). In paper III the spectral curves obtained from the aortic outflow tract were digitized by hand on a Hipad Digitizer (Model DT 11 H, Houston Instruments, Austin, Texas, USA) interfaced to an IBM-compatible computer, and the time velocity integrals were calculated using custom made data programs.

The time interpolation procedure between the velocity data from sequentially recorded flow maps was the same in all papers. The position and velocity of each point in the flow velocity maps relative to the R-wave of the electrocardiogram were known for each flow sweep, and linear interpolation between the velocities from

each sweep was done. Thus, the interpolation varied across the sector to adjust for the sweep time and resulted in an estimate of the cross sectional flow velocity profile at a single point in time.



**Fig.2.** Position-time array from consecutive and increasingly delayed flow maps. Dense lines indicate each sweep at a given radial distance from the transducer. Dense point indicate the position and time of interest (x,t).

 $T_s$  = duration of one flow sweep. L = length of one sweep. X = length of sweep from start to position (x). k = sweep number.  $t_k, t_{k+1}, \ldots$  = time at start of sweeps number k, k+1,...relative to the trigger signal

The equation for the time velocity interpolation was:

$$v(x, t) = v_k(x) \cdot (1 - a) + v_{k+1}(x) \cdot a$$

where  $a = \frac{t - k\Delta t - \frac{X}{L} \cdot T_S}{\Delta t}$  and  $0 \le a < 1$ .  $\Delta t = t_{k+1} - t_k =$  the relative increment in the delay between the trigger signal and the onset of the sweep from one heart cycle to the next.

a = 0 when the position x at time t corresponds to the co-ordinates of a recorded profile, and  $a = \frac{t - t'_k}{\Delta t}$  when the position does not correspond to the coordinates of a recorded profile (fig. 2).

In papers I, II and III this procedure was done by use of a conventional spreadsheet programme (Microsoft Excel, Microsoft Corporation, Redmond,

Washington, USA), whereas in papers IV and V this procedure was implemented in the TransDisp programme.

The cross sectional flow velocity profiles were in papers I and III constructed from an arc at defined depths of the displayed color flow maps. In papers II, IV and V the profiles corresponded to straight lines drawn on the displayed color flow maps.

Adjustments of the power threshold were allowed with the postprocessing facilities of the digital ultrasound data. This reduced the loss of velocity information that otherwise occurred at some sample volume positions.

#### Statistical methods

Results were given as ranges with the respective mean values and standard deviations. The method of Bland and Altman was used to describe agreement between two methods (paper II) or between two series of data with the same method (paper V) <sup>55</sup>. Mean differences between two data series and the standard deviations of the differences were calculated. To describe changes in the results obtained within the same group of patients during different recording conditions (paper III), the mean values and confidence intervals were given <sup>56</sup>. To test for possible differences between two or more groups of data the t-test was used and, when appropriate, it was adjusted for multiple comparisons by the Bonferroni method <sup>57</sup>.

### Results

With access to digital two-dimensional Doppler ultrasound data, postprocessing of two-dimensional flow velocity maps was possible without any loss of velocity resolution. A method for time interpolation of sequentially recorded two-dimensional flow velocity data was developed in paper I. With this method the distortion of the recorded flow velocity due to the time needed by the ultrasonograph to update each two-dimensional flow velocity map, was compensated for. Instantaneous cross sectional flow velocity distributions were constructed from serially recorded flow velocity maps with increasing delay from the onset of flow from one flow map to the next.

The method was applied to early mitral flow recorded from an apical four chamber position in 10 normal subjects. The velocity distribution against time was plotted from the calculated time corrected cross sectional flow velocity profiles. A considerable and variable skewness of the cross sectional flow velocity profiles was found. To quantify this variability the velocity at peak early mitral flow and the cross sectional mean velocity at the same time as well as the maximum and the cross sectional mean time velocity integral were estimated in each subject. At peak flow the maximum overestimated the cross sectional mean velocities with a ratio ranging from 1.2 to 2.2 at the mitral leaflet tips, and from 1.2 to 2.1 at the mitral annulus. The corresponding ratios for the time velocity integrals from early mitral flow ranged from 1.2 to 2.2 and from 1.3 to 1.7 at the leaflet tips and at the annulus, respectively. The highest flow velocities were mainly located along the anterior mitral leaflet or on the septal side of the central line of the orifice, whereas the maximum time velocity integrals were found more centrally in the orifice.

In paper II, the method developed in paper I was compared with an invasive method for the assessment of cross sectional flow velocity distributions. A reasonable agreement between the two methods was found. Mean difference between the two methods ranged from 1.4 cm/s to - 3 cm/s with standard deviations for the mean differences ranging from  $\pm$  3.4 cm/s to  $\pm$  6.9 cm/s within sample sizes

of 130 to 234 separate values. These velocities were recorded from pulsatile flow with maximum velocities ranging form 32 cm/s to 71 cm/s.

The effect of changes in the heart rate and cardiac stroke volume was studied in six patients with complete heart block and atrial fibrillation who were dependent on cardiac pacemakers (paper III). With an increase in heart rate from 60 beats per minute to 100 beats per minute the mean calculated cardiac stroke volume decreased with 28.7 % as obtained from time velocity integrals recorded in the aortic outflow tract. The decreases in maximum and mean cross sectional time velocity integrals from the mitral orifices at the level of the leaflet tips, were 20.5 % and 16.9 % respectively. The decrease in cardiac stroke volume with increased heart rate did not change the visual appearance of the flow distributions in individual patients. Neither the ratios of the maximum to the mean cross sectional time velocity integrals did change in the individual patient. The ratios of maximum to cross sectional mean velocity at the time of peak flow ranged from 1.3 to 1.9 and the ratios for the time velocity integrals ranged from 1.4 to 1.8.

In twenty patients with mitral valve disease, ten with mitral regurgitation and ten with mitral stenosis, a similar range of variations was found in ratios of the maximum to the cross sectional mean flow velocity at the time of peak flow as well as in the ratios of the maximum to the mean cross sectional time velocity integrals from early mitral flow ( paper IV). In mitral regurgitation, the cross sectional flow velocity profiles at the tip of the mitral valve leaflets were significantly more skewed than at the annulus and near the orifice in patients with mitral stenosis. The locations of the maximum flow velocities in individual patients varied more in both patient categories than in the normal subjects studied in paper I. The maximum time velocity integrals were located more centrally in the orifice than the maximum velocities at peak flow.

The inter- and intraobserver variability of the method was studied in ten normal subjects in paper V. The ranges of the maximum to the mean cross sectional flow velocity ratios and the maximum to the mean cross sectional time velocity integrals, were somewhat smaller than in the group of normal subjects in paper I, but the individual variables were within the same range. The limits of agreement were

not significantly different between the respective inter- and intraobserver comparisons performed. The widest limits were found for the interobserver comparisons where each observer analyzed their own recordings. The limits of agreement, defined as two times the standard deviation of the mean differences, ranged from 6.5 % to 34.5 % of the calculated sample mean values.

### Discussion

The presence of plug flow, i.e. an equal instantaneous flow velocity distribution across the orifice is one of the basic assumptions of volume flow calculations from velocity recordings in an orifice with known cross sectional flow area <sup>30</sup>. Several authors have applied this principle to mitral blood flow in man <sup>13, 14,</sup> <sup>16, 19-27</sup>. Some have mentioned the error which an uneven or skewed velocity profile may cause on the volume flow estimate <sup>13, 14, 22, 23, 25, 27</sup>, but, according to the authors knowledge, only one work attempting to verify the presence of a flat flow velocity profile has been published <sup>14</sup>. Others have assumed the findings in a canine experimental model to hold true also in man<sup>23, 25, 27</sup>. In the study by Taylor and Whamond <sup>34</sup>, using the Pitot principle, a basically flat velocity profile was observed at the level of the mitral annulus throughout diastole, and a zone of high shear only near the margins of the valve. Also at the level of the free cusps a flat flow profile was seen during the rapid filling phase, whereas the profile became skewed during mid and late diastolic filling with the highest velocities occurring anteriorly in the orifice. The results from the present work differ from the findings with the invasive technique. This might be due to different species studied and to the different methods used. The effect of our findings on volume flow estimates from pulsed Doppler recordings is uncertain since the effect of recording site within the orifice, the Doppler sample volume size and area estimates, are all important contributors to the results of such calculations. Most likely the presence of a skewed cross sectional flow velocity profile tends to cause an overestimate of the cross sectional average velocity and thus result in overestimation of volume flow <sup>22</sup>.

The influence of variably skewed flow velocity profiles on the use of pulsed Doppler ultrasound to record mitral flow velocities in order to characterize the diastolic function of the left ventricle, is unknown. The measurements have mainly been based on empirically derived variables regarding the shape of the flow velocity curves and the time intervals of the flow events. Complex patterns of relaxation of the left ventricular walls with local pressure differences varying with time and variable properties of the left atrium markedly influence the instantaneous pressure

gradient between the left atrium and the left ventricle. At any given moment this pressure gradient is the only force leading to the propulsion of blood from the atrium to the ventricle. Thus, the local pressure variations and the shape of the flow channel in addition to the properties of the blood are the determinators of the flow velocity distribution within the flow channel <sup>58</sup>. Despite limitations transmitral flow velocity recordings with the pulsed Doppler technique have proved to be of great value in the characterization of diastolic dysfunction in the clinical settings <sup>59-61</sup>.

The application of conventional continous wave Doppler recordings for estimation of pressure drop across stenotic or regurgitant orifices is not likely to be influenced by our findings. In such cases the main interest is the recording of the highest, instantaneous flow velocities to be used for the calculation of pressure drops  $^{62}$ .

The access to digital velocity information allowed improved accuracy of velocity recordings compared to the technique used to display conventional color flow maps. The color encoded flow velocity data as they are displayed on a monitor have a velocity resolution limited to the number of colors used to display the range of recordable velocities. Descriptive reports on cross sectional flow velocity distribution are therefore likely to be hampered by a poorer velocity resolution when video decoding of the displayed color flow velocity maps is used instead of the digital velocity information used in the present studies. In addition each of the displayed colors of the flow maps have to be calibrated against the color bar indicating the velocity ranges of each instrument setup during the actual recording.

Since the velocities change during the time it takes to build up a color flow scan, the effect of the sweep time cannot be ignored when the cross sectional flow velocity distribution is described. When recording mitral flow velocities, a flow sector angle of  $30^{\circ}$  was necessary in most subjects to map the whole cross sectional flow area from an apical four chamber view. With an acceleration of blood flow of up to  $10 \text{ m/s}^2$  in the early mitral inflow, and with the highest frame rate at a high pass filter setting of 20 cm/s, the change in recorded flow velocities from one side of the sector to the other side would be up to 40 cm/s. Thus a considerable artificial

skew results when recordings in pulsatile flow are used for construction of cross sectional flow velocity profiles and the effects of the sweep time are neglected.

#### Sources of error

Small variations in transducer position were likely to occur from one recording session to the other and thus might influence the results in papers III and V. During each recording the transducer location was assumed to be steady. Albeit small variations in location of the visualized plane might have occurred during recording this was not considered a major source of error.

During contraction and relaxation the heart changes both its shape, location and axis in the thorax and thus relatively to the external location of the ultrasound transducer <sup>28</sup>. These changes were not compensated for in the recordings of the present studies since such changes are inherent in the commonly used methods for Doppler ultrasound recordings. The line along which the cross sectional flow velocity profiles were obtained could possibly be changed with the use of the TransDisp programme, but fixed depths and orientations of this line were defined at the time of maximum valvular leaflet excursion in all recordings.

With held respiration the heart rate is likely to increase, but this was not considered a problem in the present studies since the periods of held respiration were short and the possible changes in heart rate would most likely appear in the later parts of the recording periods when blood flow velocities were low.

The trigger signal and the electrocardiogram in papers I, III, IV and V and an electronic pulse curve in paper II, was recorded simultaneously with the Doppler and tissue recordings. Due to the possible errors with manual adjustment of the trigger intervals, control measurements of the R-R-intervals and the trigger intervals were measured on hardcopies obtained from the videotape recordings

#### Limitations

The main limitation of the studies in papers I, III, IV and V was the use of only one plane for the evaluation of the cross sectional flow velocity profiles. The plane corresponding to the four chamber view was selected since this is commonly used with the combined Doppler echocardiographic technique. Thus, the possible variations of the profiles in other planes were not investigated. However, rotation of the ultrasound transducer to obtain velocity recordings from more than one plane would have introduced uncertainty of the exact location of the central axis from one plane to the other.

The description of mitral flow velocity distribution during diastole was limited by the exclusion of the late mitral flow due to atrial contraction in papers I, IV and V. The trigger function of the ultrasonograph was unstable when the duration of the time lag from the R-wave of the preceding heart beat to the onset of the delayed flow map exceeded 1.2 s. Hence recordings from subjects with low heart rates would become dubious concerning the late part of diastole. Possibly, this problem could have been eliminated by the use of an external trigger unit with an adjustable delay of the electrocardiographic signal <sup>63</sup>. If the late mitral flow had been included, the recordings would take longer time, and some patients would be unable to hold their breath.

With the development of the data transfer method and the TransDisp programme, the mode of assessment of the cross sectional flow velocity profiles changed. In papers I and III the profiles were constructed from an arc at a defined depth of the flow velocity maps whereas in papers II, IV and V the cross sectional flow velocity profiles were processed along a line drawn on the flow velocity maps with the TransDisp programme. Although the methods are principally different, the effect on the results should be small as the flow sector angle in the actual studies was 30°.

The linear time interpolation between sequentially delayed flow maps assumed no beat to beat variation in the flow pattern. Thus, only subjects with regular heart rhythm are suitable for such studies.

The high pass filter settings were selected to give optimum flow velocity maps at acceptable sweep times. Velocities below the high pass filter limit were not recorded and an artificial loss of velocities located close to the leaflets and at the very start of mitral flow as well as at the cessation of early mitral flow was introduced. The effect of the lost flow velocity data was considered to be small both at the leaflet margins and at the start of mitral flow. At the cessation of early

mitral flow the velocity loss varied with the duration of the diastole and onset of the late diastolic flow due to atrial contraction.

The applicability of our method at present is limited to the description of cross sectional flow velocity profiles. The method cannot be used for volume flow calculations since the recorded flow sectors only were obtained from one plane oriented in parallel to the blood flow through the mitral orifice. Thus the maximum and mean cross sectional flow velocities as well as the maximum and mean cross sectional values for the time velocity integrals were not representative for the whole cross sectional blood flow area.

Theoretically, the method could be modified in two ways to make it more suitable for volume flow calculations. With a fixed rotation axis the velocity profile of the whole flow area could be obtained, and an accurate estimate of volume flow would be possible. Unfortunately, this method would be too time consuming to be of practical use with the present data pogrammes and equipment.

Another way of obtaining information on blood flow velocities from the whole flow area would be to use a tissue and flow sector plane with known oblique angle to the long axis of a tubular flow channel. However, the width of the mitral orifice compared to the length and non-uniformity with time of this flow channel makes such approaches difficult. The necessary angle between the blood flow direction and the ultrasound beam would be too large for precise velocity estimates.

Recently, the use of the proximal isovelocity surface area for the calculation of volume flow through regurgitant valves has gained interest <sup>64</sup>. This method could easily be applied to our technique for the calculation of time corrected flow velocity profiles to identify a surface of equal velocities of the flow upstream to the diseased valve.

### Conlusions

1. With the use of digital Doppler ultrasound data from two dimensional flow velocity maps, a method for the construction of time corrected cross sectional flow velocity distribution was established.

2. The accuracy of the method was compared to an established invasive method in an in vitro model. The differences between the two methods were within reasonable limits.

3. The cross sectional flow velocity profiles were variably skewed both in normal subjects and in patients with mitral regurgitation and patients with mitral stenosis.

4. Changes in heart rate and stroke volume did not introduce systematic changes in the skewed cross sectional flow velocity profiles when the heart rate was varied from 60 to 100 beats per minute in pacemaker dependent patients.

5. The inter- and intraobserver comparisons of the method gave acceptable limits of agreement regarding the recording, the analyzing procedure, and the combination of both.

6. The finding of a skewed flow velocity profiles in early mitral flow should be born in mind when volume flow calculations are based on Doppler ultrasound recordings from only a small area within the mitral orifice. The recorded flow velocities might not be representative and thus result in significant errors.

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## Errata

### Paper I:

- p 179: Ledgend figure 2, line 12 from top; d1 is misspelled (dl).
- p 180 -1: Figueres 4a and 5a have changed place.
- p 181: Text in the right column line 8 from top; mean is misspelled (men).

### Paper II:

p 462: Text in the right column line 11 from top; 5 ms is misspelled (5 m/sec).

## Paper III:

p 79: Text in the left column line 11 from top; *Bonferroni* is misspelled (*Bonferoni*).

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## Cross sectional early mitral flow velocity profiles from colour Doppler

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SUMMARY Instantaneous cross sectional flow velocity profiles from early mitral flow in 10 healthy men were constructed by time interpolation of the velocity data from each point in sequentially delayed two dimensional digital Doppler ultrasound maps. This interpolation allows correction of the artificially produced skewness of velocities across the flow sector caused by the time taken to scan the flow sector for velocity recording of pulsatile blood flow. These results suggested that early mitral flow studied in an apical four chamber view is variably skewed both at the leaflet tips and at the annulus. The maximum flow velocity overestimated the cross sectional mean velocity at the same time by a factor of  $1\cdot 2-2\cdot 2$ . Also the maximum time velocity integral overestimated the cross sectional mean time velocity integral to the same extent.

This cross sectional skew must be taken into account when calculation of blood flow is based on recordings with pulsed wave Doppler ultrasound from a single sample volume.

Pulsed wave Doppler has been used to record the flow patterns in non-stenotic mitral valves.<sup>1-3</sup> The method has an accurate time resolution, but the velocities are recorded from only a small area of the valve orifice. If the velocity varies across the orifice a recording from one sample volume may differ from the mean cross sectional velocity. Recently colour flow Doppler has been used to describe flow velocity patterns.<sup>4-6</sup> This method has accurate spatial resolution, but the poor time resolution might introduce errors in the measurement of pulsatile flow because of the sweep time across the flow sector, which is needed to update the colour flow maps.

To overcome the limited spatial information given by pulsed wave Doppler and the poor time resolution of colour flow Doppler a new method was developed. Digital Doppler ultrasound two dimensional flow maps, obtained with the ultrasound beam directed in parallel to the blood velocities, were used to construct instantaneous flow velocity profiles across the mitral orifice.

The technique was used to examine mitral flow in

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early diastole in healthy men. We examined these flow velocity profiles to estimate the error that may occur with pulsed wave Doppler when a limited sample volume is used to measure the mean velocity across the orifice.

### Patients and methods

Ten healthy men, aged 12 to 42 years (mean 31 years), consented to the study. None had clinical, auscultatory, electrocardiographic, or echocardiographic evidence of heart disease.

The ultrasound measurements were made with a CFM 700 system (VingMed Sound). This is a combined cross sectional echocardiographic and two dimensional Doppler flow velocity system where the flow sector is constructed by colour coding the velocity information from 64 sample volumes along each of 64 sequentially transmitted ultrasound beams in each flow velocity map. The velocity in each sample volume is calculated by an autocorrelation function on the frequency and the intensity of the backscattered ultrasound signal.<sup>78</sup> We used a 3 MHz transducer with the high pass filter set at 21 cm/s, and by scrolling the baseline the upper velocity limit was 120 cm/s. The lateral resolution of the ultrasound beam, defined as a 50% decrease in

Samstad, Torp, Linker, et al.

backscattered signal from the centreline of the beam, was  $2 \cdot 1 - 2 \cdot 5$  mm at a depth of 8 cm from the transducer when the flow sector angle was set to  $30^{\circ}$ .

Each ultrasound beam is incrementally delayed relative to the preceding beam because of the time needed to send and receive several pulses before a new beam can be sent in the next direction. The sweep time of each flow map with a flow sector angle of 30° varies from 40 to 114 ms for different instrument set-ups and transducer. The actual sweep times are measured directly on the transducer controller inside the instrument. The flow sector can be moved by a track ball both laterally and radially in relation to the tissue sector. The width and the radial extension of the flow sector can also be adjusted while the  $64 \times 64$  sampling volumes are maintained. The distances from the transducer to the areas of interest in the tissue and flow velocity maps are measured accurately by the analysis facilities of the instrument.

The men were examined in the left lateral recumbent position. The transducer was located at the apical window to give a four chamber view of the heart. Adjustment of the position and direction of the transducer and of the orientation of the flow sector reduced to a minimum the angle between the radial direction of the flow sector and the main direction of the mitral flow. The septal and lateral parts of the mitral annulus were visualised, and the sector plane was adjusted in the anterioposterior plane until optimal flow signals were obtained from the inflow channel. During data acquisition the patients were asked to stop breathing in passive end expiration with open airways.

Electrocardiographically triggered flow maps of the mitral area were made from sequential beats, and the start of the flow sweep relative to the R peak was increasingly delayed with increments of 20 ms from one beat to the next. The increases in sweep delay were adjusted manually. The first sweep was recorded before the start of passive atrioventricular flow and the last sweep after onset of flow caused by left atrial systole. The number of sweeps ranged from 13 to 19 (mean (SD)  $16\cdot1$  ( $2\cdot3$ )) in the ten men. The serial time gated recording of these flow sweeps obtained from each man was used for analysis of the flow patterns both at the mitral annulus and at the leaflet tips. None of the recording periods exceeded 25 seconds.

The ultrasound recordings were transferred to an external computer as raw Doppler data from the front end of the CFM 700 in real time or as digital velocity data from the replay memory of the instrument (fig 1). In addition, the recordings were stored on videotape.

In subjects 1 to 4, the raw colour Doppler data were transferred from the front end of the instrument



Fig 1 Ultrasound system. Solid line represents the signal passage from the transducer (upper left) to the final presentation as cross sectional tissue and colour flow map on the monitor of the instrument (upper right). Four major levels of signal processing in the instrument are: (1) Instrument front end connected to the transducer. A custom made portable ultrasound data grabber and interface (PUDGI) capable of transferring the raw ultrasound data in real time to an external computer can be connected to the front end. The real time transfer of the ultrasound data enables post-processing of the raw digital Doppler flow data without its being influenced by the processing units of the instrument. (2) Data processing unit. The tissue data (t) and the Doppler colour flow data (c) are processed separately before the data are passed to the scan converter (4). (3) Digital replay memory with two megabyte storage capacity. The processed data on tissue and Doppler colour flow are passed to the replay memory of the instrument in parallel with the data transfer from the processing unit (2) to the scan converter (4). At this level the tissue and Doppler colour flow data are handled separately and the replay memory is continuously updated as new data are passed through the system, with a simultaneous erasing of the oldest data in the memory. In freeze mode of the instrument the content of the digital replay memory can be replayed from the monitor for measurements and tape recording. These data can also be transferred to an external computer for the analysis performed in this article. (4) Tissue and colour flow images are mixed in the scan converter for combined presentation on the monitor. The Doppler colour flow sector is overlayed on the tissue sector from the same transducer sweep cycle.

via a custom made ultrasound data grabber and interface (PUDGI) to a Stride 460 computer (Stride Micro, Reno, NV). The raw two dimensional Doppler data were processed by a computer program that emulated the velocity estimation in the ultrasound instrument, and the velocity data were presented as a colour flow map displayed on a monitor or as velocity curves representing the velocities from each depth along an arc across the 64 beams. The velocity data were stored for further processing (fig 1).

The recordings from subjects 5-10 were transferred from the replay memory of the ultrasound

### 178

### Cross sectional early mitral flow velocity profiles from colour Doppler

instrument to an external computer (IBM PC compatible). At this level of data processing the Doppler data are available as digital velocity information from each of the 64 times 64 points of the flow sector from each recorded map. The selected number of consecutively recorded maps from each patient could be transferred by custom software in the ultrasound instrument. The velocities along an arc of the 64 beams at defined depths from the recordings could also be transferred from these files to a standard data file for further processing.

These standard data files, containing information on the instrument set-up as well as the digital Doppler data, were loaded into a commercial spreadsheet program (Microsoft Excel, Microsoft Corporation) where the calculations needed to correct for the sweep time and generate undistorted velocity profiles were made.

In some of the recorded maps, velocity data from some points along the arc of the ultrasound beams were missing. These "holes" were regarded as artefacts introduced by the instrument. The missing values were corrected in the spreadsheet program by comparing the velocity data close to the "hole" and replacing the missing values with the average of the two neighbouring values from the same sweep before the time interpolation procedure.

Both transfer procedures give rapid collection of high quality flow velocity data unaffected by errors introduced by the display system, video recorder, or re-digitisation of a colour coded display.

Any of the 64 arcs across the flow sector can be used to generate velocity profiles. The depth from the transducer to the displayed cardiac structures of the tissue sector can be measured from the actual recording by the replay memory of the instrument.

Since the mitral flow is pulsatile, the sweep time from one side of the flow sector to the other distorts the velocity profiles constructed from arcs of sample volu nes across the flow sector. To compensate for this distortion, data obtained from sequentially delayed flow sweeps were interpolated. Each sweep of the ultrasound beam was triggered by the R wave of the electrocardiogram. Consecutive sweeps were delayed by 20 ms in relation to the previous one (fig 2 b and c). We excluded recordings where the RR intervals of the various heart cycles deviated more than 20 ms from the median.

Thus the position and velocity information from each point along the selected arcs relative to the R wave of the electrocardiogram were known for each flow sweep, and linear interpolation between the velocities from each of the sequentially delayed recordings was done. The interpolation varied across the arc to adjust for the sweep time and resulted in an estimate of the cross sectional flow profile at a single



Fig 2 (a) Schematic drawing of the heart in apical four chamber view. The mitral flow velocity distribution in this example is assumed to be flat. The ultrasound Doppler two dimensional sector is 30°; the two dimensional Doppler ultrasound sweep direction is from right to left, sweep time = 50 ms. Horizontal arrows indicate the depths of cross sectional flow profiles in this study. (b) Pulsed wave Doppler recording of the pulsatile flow in the mitral orifice at both levels with overlayed velocity changes during a recording period (s) of 50 ms, and where the recording period is sequentially delayed (d) by 20 ms relative to the flow start from one flow period to the other; dl = 0 ms, d2 = 20 ms, and d3 = 40 ms. (c) Velocity traces across the width of the mitral orifice in panel (a) as obtained when recorded with the ultrasound Doppler two dimensional system. Velocities are given along the y axis and the position in the mitral orifice along the x axis ( $a = anterior \ leaflet$ , p = posteriorleaflet). Numbers 1 to 3 represent sequentially delayed two dimensional sweeps of the flow pulses 1 to 3 in (b). The duration of each sweep is 50 ms. Note the artificial skewing caused by the lag in data collection. (d) Instantaneous flow velocity distribution across the width of the orifice in panel (a). Velocities are given along the y axis, and position in the mitral orifice along the x axis (a = anterior leaflet,p = posterior leaflet). This flow profile is calculated by linear time interpolation of the velocity traces 1 to 3 in panel (c), at 50 ms from start of flow.

point in time (fig 2d). Since the time lag of the updating of the colour flow map is compensated for by the calculation procedure, we called this calculated cross sectional flow velocity distribution *the* 

### 180

instantaneous flow velocity profile. An instantaneous flow velocity profile could be calculated for any time in the flow cycle and at any depth of the two dimensional Doppler flow velocity sector and the results displayed as a three dimensional plot for each depth (fig 3). We calculated the instantaneous flow velocity at the leaflet tips and at the mitral annulus in all 10 men, and measured the actual depths at the time of maximum separation of the mitral leaflets in early diastole.

### STATISTICAL ANALYSIS

Results are given as ranges and sample means (SD).

### Results

The results were plotted as velocity profiles versus time to give a three dimensional presentation of the





Fig 3 Plots of instantaneous early mitral flow velocity profiles against time. Axis scaling and orientation are shown at the top of the figure. Plots a and b are from subject number 2, recorded from the level of the leaflet tips, (a) and at the level of the mitral annulus (b). Plots (c) and (d) are from subject number 7 at the level of the leaflet tips and annulus respectively. In these two healthy men the instantaneous flow profiles at the leaflet tips are skewed, but the maximum velocities are at different positions in the valve orifice—in subject 2 at the posterior leaflet and in subject 7 at the anterior leaflet. The velocity profiles were skewed at the level of the mitral annulus in both men, but the highest velocities were recorded at the anterior leaflet.

### Samstad, Torp, Linker, et al.

data. The profiles were to some extent skewed in all subjects, both at the annulus and at the tip of the mitral valve leaflets. The plots in fig 3 show different orientations of the skew in two patients. In patient 2 the skew is toward the posterior leaflet, while in patient 7 the skew is toward the anterior leaflet. At the level of the annulus the highest velocities were recorded anteriorly in both men.

The maximal instantaneous velocity versus the simultaneous cross sectional mean velocity gives an indication of the degree of skewness at the time of peak flow. The difference between maximum velocity and cross sectional mean velocity at the leaflet tips varied from 14 cm/s in subject 2 up to 41 cm/s in subject 6 (table). The mean differences for all subjects were 24.4 cm/s and 23.1 cm/s at the level of the leaflet tips and at the annulus respectively. Figure 4 shows the relative locations of the maximum velocity as a proportion of the cross sectional mean velocity at the same time for each man at the levels of the leaflet tips and the annulus.

The time velocity integral is the integral of velocity over time for a specific point in the arc. This is the value used to estimate volume flow when recording with pulsed wave Doppler from a single sample



Fig 4 (a) Ratio of the maximum velocity to the mean cross sectional velocity at the time of maximum flow velocity of early mitral flow, at the leaflet tips (solid bars) and at the annulus (patterned bars). (b) Site of the maximum velocity within the mitral orifice is shown for each subject at the level of the tips (solid dots) and the annulus (open circles). Leaflet margins are indicated as solid vertical lines.

| No   | Age<br>(yr) | HR<br>(beats/min) | Velocity (V) (cm/s) |        |         |              | Time-velocity integral (1) (cm) |        |         |             |
|------|-------------|-------------------|---------------------|--------|---------|--------------|---------------------------------|--------|---------|-------------|
|      |             |                   | Tip                 |        | Annulus |              | Tip                             |        | Annulus |             |
|      |             |                   | Max V               | Mean V | Max V   | Mean V       | Max I                           | Mean I | Max I   | Mean l      |
| 1    | 38          | 55                | 59                  | 36     | 80      | 57           | 6.2                             | 3.7    | 7.5     | 4.9         |
| 2    | 42          | 41                | 79                  | 65     | 82      | 65           | 12.0                            | 10.0   | 11.0    | <b>8</b> ·7 |
| 3    | 32          | 76                | 70                  | 33     | 57      | 34           | 6.8                             | 4.7    | 5.6     | 4.1         |
| 4    | 28          | 67                | 50                  | 32     | 55      | 26           | 8.1                             | 5.6    | 6-8     | 4·7         |
| 5    | 42          | 60                | 80                  | 57     | 67      | 51           | 10.3                            | 7.6    | 7.7     | 6.0         |
| 6    | 33          | 68                | 75                  | 34     | 66      | 39           | 11-3                            | 5.2    | 10.0    | 6.0         |
| 7    | 28          | 56                | 55                  | 37     | 58      | 37           | <b>6</b> ∙8                     | 4.6    | 7.5     | 4.8         |
| 8    | 34          | 59                | 73                  | 54     | 77      | 52           | 10-1                            | 6.9    | 7.2     | 5.1         |
| 9    | 25          | 58                | 80                  | 60     | 82      | 66           | 11-1                            | 8.6    | 8.9     | 6.4         |
| Ō    | 12          | 74                | 77                  | 46     | 74      | 40           | 8.7                             | 6.4    | 8.3     | 4.9         |
| Mean | 31          | 61                | 69.8                | 45.4   | 69.8    | <b>46</b> ·7 | 9.1                             | 6.3    | 8.1     | 5.6         |
| SD.  | 0           | 10                | 11.1                | 12.6   | 10.6    | 13.5         | 21                              | 2.0    | 1.6     | 1.3         |

 Table
 Maximum flow velocity and time-velocity integral of early mitral inflow compared with the simultaneous mean velocity and mean time-velocity integral across the mitral orifice at the level of the leaflet tips and the annulus

Tip, measurements at the level of mitral leaflet tips; annulus, measurements at the level of the mitral annulus; HR, heart rate; Max V, maximum velocity of the early mitral flow; Mean V, cross sectional mean velocity at the time of maximum velocity at the defined level; Max I, time velocity integral from the point in the flow sector at the defined level giving maximum value of early mitral flow; Mean I, mean cross sectional time velocity integral of early mitral flow at defined depth in the flow sector.

volume. The maximum time velocity integral is the maximum found for a given arc. The mean time velocity integral is the arithmetic mean of the integral values across this arc.

The difference between the maximum and the simultaneous cross sectional mean time velocity integral varied from 1.5 cm at the annulus in subject 3



Fig 5 (a) Ratio of maximum time-velocity integral to the mean cross sectional time-velocity integral of early mitral flow at the leaflet tips (solid bars) and at the annulus (patterned bars). (b) Site of the maximum time-velocity integral within the mitral orifice is shown for each subject at the level of the tips (solid dots) and the annulus (open circles). Leaflet margins are indicated as solid vertical lines.

up to  $6 \cdot 1$  cm at the leaflet tips in subject 6 (table). The mean differences for all subjects were  $2 \cdot 8$  cm at the leaflet tips and  $2 \cdot 5$  cm at the annulus. Figure 5 shows the ratio of the maximum integral to the mean time velocity integral, and the relative location of the maximum integral within the orifice for each man at the levels of the leaflet tips and the annulus.

Heart rate ranged from 41 to 76 (men 61 (10)) beats per minute (table). All men were in sinus rhythm.

### Discussion

The results indicated that the velocity profiles, both at the tips of the mitral valve leaflets and at the annulus, are skewed to a variable degree during the early phase of the mitral flow. At the time of peak flow, the highest velocities were 1.2 to 2.2 (tip of the leaflets) and 1.2 to 2.1 (annulus) times higher than the cross sectional mean velocity. Similar results were found when the highest time-velocity integral was compared with the mean time-velocity integral across the orifice, indicating that the profiles were skewed to some extent throughout the early phase of the mitral flow. There were no clear differences in the degree of skewness at the tip of the leaflets and at the annulus. The average overestimation of the mean velocity integral that would occur if the maximal integral had been used was 49% at the tip of the leaflets and 46% at the annulus. The standard deviation, however, was larger at the tip of the leaflets (27% v 15%).

The orientation of the skew within the valve apparatus varied between individuals and in some men between the annulus and the leaflet tips (fig 4); it also varied with time (fig 3). This observation suggests that the recording of maximum flow velocity with pulsed wave Doppler ultrasound should not be guided by the location in the valve orifice at a defined depth, but by the observed maximum velocities only.

In one of the men (number 1, table) we found a higher maximum flow velocity at the mitral annulus than at the leaflet tips. This is in contrast with what is usually found with pulsed Doppler in patients and might possibly be explained by the suboptimal orientation of the plane of the sweep sector because both cross sectional profiles were obtained from the same sweeps. The small difference in maximum velocities between the annulus and the leaflet tips in four of the other men may similarly have been caused by a suboptimal anterioposterior orientation of the plane of the flow sector, but might also be explained by small differences in orifice size at the two locations.

Few attempts have been made to measure the velocity profiles of mitral flow because its location within the heart makes it difficult to measure. Invasive procedures may interfere with valvar or ventricular function and this may affect the mitral flow pattern.

We are aware of only one previous published study on the velocity profiles of mitral flow.<sup>9</sup> Taylor and Whamond used a Pitot needle to study flow through the mitral orifice in dogs. They reported fairly flat profiles of early mitral flow both at the annulus and at the tip of the valve leaflets. Taylor's results and our own may differ because we studied different species and used different techniques.

Previous estimates of volume flow based on measurements of flow velocity and flow area at the level of the mitral valve assumed a flat velocity profile.<sup>10 11</sup> Our results suggest that values based on the maximum time velocity integral tend to overestimate the mean integral. The inconsistency of the results of different studies may partly be explained by our findings of a non-flat velocity profile and partly by inaccuracies in measurements of the effective flow area.<sup>12-15</sup>

### APPLICATIONS

Colour flow Doppler provides a new way of evaluating velocity profiles within the heart because the velocity information from sample volumes located along an arc at a certain depth can be analysed. The advantage of this method is that the ultrasound beam can be oriented almost in parallel with the flow velocity. The resulting cross sectional velocity profiles will thus contain more accurate velocity information. However, the main problem is that these velocity profiles will be skewed when recordings are made of accelerating flow because of the time taken to scan the flow sector. There are several reports on flow topography based on Doppler two dimensional flow recordings.<sup>4+6</sup> One of them was an in vivo study in which the time lag of the colour Doppler technique may have introduced errors because of the changes in flow velocity during each flow scan.<sup>5</sup> So far the timing of the colour flow sweep in relation to the events during the cardiac cycle has been discussed only in relation to regurgitation jets.<sup>10 17</sup>

The present method avoids the distortion of the velocity profile caused by the time lag, making it possible to obtain accurate velocity profiles at different sites within the heart. This has important implications for volume flow calculations, especially in regurgitation and with shunts.

### OTHER METHODS

Multigated Doppler ultrasound has been used by some.<sup>18 19</sup> But with this method the flow velocity has to be recorded nearly perpendicularly to the direction of the ultrasound beam to read the flow velocity profile across the width of a flow channel. This is a disadvantage because errors in the velocity estimate increase as a function of the cosine of the angle between the blood flow and the ultrasound beam.

Magnetic resonance techniques for velocity mapping have been used on the ascending and descending aorta in healthy individuals,<sup>20 21</sup> but so far flow velocity profiles across the mitral orifice have not been reported.

In experimental settings different methods have been used, including the Pitot principle<sup>9</sup> and hot film anemometry,<sup>22 23</sup> but the invasiveness of these methods limits their use in patients. Pulsed wave Doppler ultrasound, with the ultrasound beam directed in parallel with the blood flow direction, has been used to measure flow in the ascending aorta during operation.<sup>24</sup>

### LIMITATIONS OF THE METHOD

The main limitation of the method used in the present study was that the profiles were evaluated in only one plane and from only one sequence of time gated recordings in each man. This may explain why the highest velocities were recorded at the annulus in some men. At the tip of the leaflets the highest velocities may have been outside the plane of the colour flow sector. This limitation can be overcome by stepwise rotation of the transducer to construct a series of profile maps. With current instruments and software such a procedure would be too time consuming.

Because the streamlines of the mitral flow probably ran in parallel, at least during part of diastole, and the ultrasound beams making up the Doppler colour

182

sector did not, the angle of incidence between the flow and measurement direction varies from one side of the flow area to the other. To minimise the error on profile calculations we attempted to align the centreline of the Doppler sector with the centreline of the flow. A sector angle of  $30^{\circ}$  was sufficient to cover the mitral flow in the region of interest, limiting the maximum angle of incidence to about 15%. Accordingly, an error on velocity estimates should be less than 6%. When the velocity pattern is more complicated (that is the streamlines are not parallel) or when the vector of the velocities is out of the plane of the flow velocity sector the error may be larger.

The velocity estimates at each point in the two dimensional flow map are based on calculations of the Doppler shift of the received signal from each point in the sector. In conventional Doppler recordings, fast Fourier transformation is used to give a spectrum display as well as maximum and mean estimates. Because the two dimensional flow technique has a much faster rate of data acquisition than conventional Doppler, more efficient processing of the data is required. The algorithm used by the instrument is based on calculation of the centre frequency (that is the mean frequency of the Doppler spectrum from each point in the flow sector) and intensity of the received signal based on an autocorrelation technique. If flow is not disturbed this method gives accurate velocity estimates.78

The lateral resolution of the system caused two neighbouring points in the three dimensional plots to overlap at a position where the power of the backscattered signals was reduced to 60% of the maximum power centrally in each beam (fig 3). The influence of points that were further apart was not significant. Hence the resolution of the three dimensional plots was regarded as appropriate.

The high pass filter of the instrument used was set at 21 cm/s, which means that velocities below this limit were not recorded. The upper velocity range is limited by the Nyquist frequency.<sup>25</sup> However, by moving the baseline this limit can be increased up to two times the Nyquist velocity minus the high pass filter velocity limit. We used a 3 MHz transducer with an upper velocity limit of 120 cm/s.

The two different routines for transferring the digital ultrasound data from flow sweeps introduced no differences in the calculation of flow velocities because both methods used the same algorithm to calculate velocity. Also we calculated the instantaneous flow velocity profiles in the same way in all the men—by linear time interpolation between the acquired data from the sequentially delayed flow maps.

### SOURCES OF ERRORS

Because the recording technique samples data from

several heart beats it requires exact aiming, without transducer movement during the recording period. Thoracic movement and changes in mitral flow volume caused by respiration were likely to introduce errors. So the men were asked to stop respiration in passive end expiration with open airways during data acquisition.

Changes in the selected depth of sampling caused by volume filling of the left ventricle during the recording period were not corrected because the change in location of the mitral annulus within the two dimensional flow sector was considered to be small during early diastole.

Irregularities in heart rate and rhythm, as well as the increment in the sequentially delayed two dimensional flow maps relative to the trigger marker (the R wave of the electrocardiogram signal), could also introduce errors in calculations of the instantaneous flow velocity profile.

To reduce these sources of error we checked all recordings for inaccuracies by replaying video recordings. Because the two dimensional tissue sector is updated immediately before the two dimensional flow map, changes in tissue and flow sectors relative to the heart from one heart beat to the other could be monitored.

### CONCLUSIONS

The use of digital flow velocity information from two dimensional Doppler flow maps of the early mitral flow, using time interpolation of the acquired data from sequentially delayed flow maps, provides a new method for calculation of instantaneous flow velocity profiles.

The results from our study give new information on the distribution of mitral flow velocity across the width of the mitral valve at the levels of the leaflet tips and at the annulus in the human heart. This shows that the instantaneous flow velocity profiles are variably skewed at both sample depths in an apical four chamber view. A skewed profile of early mitral flow velocity should be borne in mind when recordings from a small area in the valve orifice are used for volume flow calculations; this skewness may result in significant errors.

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# Paper II





## Instantaneous Cross-sectional Flow Velocity Profiles: A Comparative Study of Two Ultrasound Doppler Methods Applied to an In Vitro Pulsatile Flow Model

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Two methods based on different techniques for construction of cross-sectional flow velocity profiles from Doppler ultrasound signals were compared: an intraluminal method using pulsed-wave Doppler echocardiography and an extraluminal method using two-dimensional (color) Doppler ultrasound. The methods were applied to an in vitro pulsatile flow model. With the intraluminal method, pulsed Doppler recordings obtained throughout several flow pulses at different positions across a tube were digitized, and cross-sectional flow velocity profiles were obtained by matching the onset of flow velocity at the various positions. With the extraluminal method, cross-sectional flow velocity profiles were obtained by time interpolation between the digital flow velocity data obtained from several flow velocity maps. The first flow velocity map was recorded at onset of flow and the following maps were incrementally delayed with 20 msec from one flow pulse to the next. The time lag caused by the time needed to update each of the flow velocity maps was compensated for by time interpolation between the sequentially recorded flow velocity maps. The cross-sectional flow velocity profiles obtained with the two methods were compared at identical positions within the tube model at equal flow settings and throughout the pulsatile flow periods. At three different flow settings with peak flow velocity of 0.3, 0.5, and 0.7 m/sec, the difference (mean  $\pm$  SD) between the obtained velocities were  $0.01 \pm 0.04$ ,  $-0.01 \pm 0.05$ , and  $-0.03 \pm 0.07$  m/sec, respectively. The findings suggest that cross-sectional flow velocity profiles from pulsatile flow velocity recordings can be obtained equally well with both methods. (J AM SOC ECHO 1990;3:451-64.)

Noninvasive recording of blood flow velocities by use of Doppler ultrasound can easily be obtained. For volume flow measurements, however, the mean spatial velocity across a flow area is required. With

27/1/24455

a flat flow velocity profile across an orifice or vessel, volume flow can be obtained by multiplying the time velocity integral from a pulsed Doppler recording with the flow area. However, in situations where the velocity varies across an orifice or vessel, with a skewed or parabolic velocity profile, a pulsed Doppler recording from a small area may not be representative for the mean across the lumen or orifice and may result in overestimation or underestimation of volume flow. For volume flow calculations, it is therefore essential to know how the velocity profile is. In recent years several publications have dealt with this topic.<sup>1-16</sup>

Both invasive<sup>1-5</sup> and noninvasive<sup>6-11</sup> methods have been used to obtain cross-sectional flow velocity profiles. During surgery, various invasive techniques

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**Figure 1** Hydromechanical cardiovascular flow simulator. *1*, An electropneumatic unit with options for different flow settings and output for trigger pulses to the Doppler instruments. *2*, A ventricle enclosed in a chamber connected to the electropneumatic unit. By forcing gas into the chamber the ventricle "contracted" and by evacuation of gas from the chamber the ventricle "relaxed," all gas transport were controlled with the electropneumatic unit. The blood substitute entered the atrium through a tricuspid valve made of silicone rubber during diastole and was forced through a similar valve into the aorta during systole. *3*, An aorta with branching arteries (not shown) made of silicone rubber connected to the adjustable resistance units. *4*, The site of flow velocity recording. *5*, An adjustable peripherial resistance unit. *6*, A reservoir chamber, large "vein." *7*, An atrium with adjustable preload.

have been used. Taylor and Whamond<sup>1</sup> applied the pitot principle on canine mitral flow, and Seed and Wood<sup>2</sup> and Paulsen and Hasenkam<sup>3</sup> used a hot film anemometer to obtain the cross-sectional flow velocity distribution in the aorta. Others have used invasive pulsed Doppler recordings in the canine and human ascending aorta.4,5 Noninvasively, the flow velocity distribution in the human ascending aorta was studied with multigated pulsed Doppler by Jenni et al.,<sup>6,7</sup> and the color Doppler technique has been used to describe the flow pattern in the right atrium, in the left ventricular outflow tract, and in a flow simulator.8-10 Time interpolation between sequentially delayed two-dimensional color Doppler flow maps has been used to obtain instantaneous crosssectional flow velocity profiles of early mitral flow in normal subjects.<sup>11</sup> Magnetic resonance imaging has also been used to describe flow velocity patterns in the human ascending aorta.<sup>12,13</sup>

None of these methods have been compared with each other for cross-sectional flow velocity distribution. One of the methods has been compared with electromagnetic flow probes for volume flow measurements,<sup>15,16</sup> but these flow probes cannot be used for comparison with methods to obtain crosssectional flow velocity profiles. These flow probes record the instantaneous *mean* flow velocity across a flow channel, and no detailed information on the instantaneous cross-sectional flow velocity distribution is obtained.

In this study a noninvasive method that used twodimensional color-coded Doppler ultrasound<sup>11</sup> was compared with an invasive method that used pulsed Doppler ultrasound<sup>5</sup> for obtaining cross-sectional flow velocity profiles across an in vitro flow channel with pulsatile flow. The flow velocities recorded with pulsed Doppler have excellent time resolution, and by recording flow velocities at several positions across a diameter and matching the start of each recorded flow pulse, instantaneous flow velocity profiles can be constructed.<sup>5</sup>

Two-dimensional Doppler ultrasound gives the spatial distribution of velocities over a wide sector in one plane. The time resolution is limited by the frame rate, which is usually on the order of 5 to 15 frames per second. The lack of time resolution was compensated for by time interpolation between sequentially recorded flow velocity maps from several flow pulses. The start of the first flow velocity map was matched to the start of the pulsatile flow and the start of the following maps were incrementally delayed from one flow pulse to the next.<sup>11</sup>

Both methods were used to obtain instantaneous cross-sectional flow velocity profiles within a tube connected to a hydromechanical flow simulator able to produce pulsatile flow with various peak flow velocity settings.

### MATERIAL AND METHODS

### Cardiovascular Hydromechanical Simulator

The cardiovascular simulator consisted of a "ventricle" and an "atrium" separated by a valve, connected to an "aorta" by way of a tricuspid synthetic valve (Figure 1). From the aorta, branches of minor vessels with increased resistance were interpositioned before they were drained by a large delay tube ("vein") connected to the atrium. The "ventricle" was made of elastic silicon rubber and was positioned in a rigid container and driven by an electropneumatic unit.<sup>17</sup> All vessels were elastic silicone rubber tubes.

With the control unit, the ventricular maximum pressure, the rate of pressure increase and decrease, and the duration of systole and diastole could be adjusted. Peripheral vascular resistance could also be adjusted to obtain different flow velocities within the aorta.

## Blood Substitute Used in the Hydromechanical Simulator

Distilled and evaporated water was mixed with glycerol at a ratio of 5.05 to 1 to obtain a specific weight approximating that of whole blood  $(1.06 \cdot 10^3 \text{ kg/m}^3)$ . Dextran microsphere particles (Sephadex G-25 superfine 100, Pharmacia LKB, Bromma, Sweden) were suspended in distilled water, and small volumes were added to the fluid in the hydromechanical simulator to obtain strong Doppler reflections.

Flow velocity recordings within the silicone tube were made in the "descending aorta" of the flow simulator (Figure 1). The two Doppler ultrasound devices were arranged to record the velocity distribution from the same diameter across the tube, 40 cm distal to the end of the aortic arc (Figure 2). The internal diameter of the tube at this site was 22 mm. All drainage of blood substitute was distal to the site of measurements.

With the extraluminal method the combined twodimensional Doppler ultrasound imaging transducer was positioned outside the aorta. An angle of 45 degrees between the plane of the flow sector and the centerline of the tube was used, the centerline of the flow sector was positioned in the midline of the tube (Figure 2). The width of the flow sector was 60 degrees when the color flow sector covered the large diameter of the tube and 30 degrees when only the central part of the tube was investigated.

With the intraluminal method the pulsed-wave Doppler transducer was embedded in epoxy resin on a needle that was introduced through a minor branch, "an artery," at an angle of 90 degrees to the aorta. The direction of the ultrasound beam was perpendicular to the axis of the needle, and the device could be positioned at any point of the large diameter of the "aorta" (Figure 2). The needle on which the pulsed Doppler transducer was mounted could be clearly seen with the two-dimensional imaging instrument when introduced into the lumen of the tube.

### Ultrasound Recordings

**Instrumentation.** With the intraluminal method the 10 MHz transducer was connected to a Doppler ultrasound meter (SD 100, VingMed Sound, Oslo,



Figure 2 A, Arrangement of the extraluminal color Doppler transducer relative to the tube. In the left panel the extensions of the two-dimensional Doppler sectors of 60 degrees and 30 degrees within the tube are shown. In the right panel the angle of incidence between the plane of the flow sector and the tube is shown. Arrows at the top indicate the flow direction; stipled arrows indicate the level of velocity recordings for comparison with the invasive method.  $\emptyset = 22$  mm indicates the width of the tube. B, Arrangement of the intraluminal pulsed Doppler transducer relative to the tube. In the left panel the same projection is seen as in the left panel of A. The transducer was inserted into the tube through a valve in the branching "artery" and the device was moved from left to right in steps of 2 mm. In the right panel the intraluminal transducer is indicated by the *closed circle* in the tube. Arrows at the top indicate flow direction; stipled arrows indicate the level of velocity recordings for comparison with the invasive method. The pulsed Doppler beam was directed in parallel with the flow direction, and the velocity sampling was made 3 mm upstream from the transducer.

Norway). Velocity sampling was performed 3 mm upstream to the probe to avoid retrograde influence from the probe itself. The minimum sample volume length, 1 mm, was used. The sample volume length was equal to the axial resolution within the tube because the ultrasound beam was aligned with the tube axis. The lateral resolution within the tube was nearly equal to the diameter of the piezoelectric crystal, 1 mm, at the depth of recording. The spectrum high-pass filter was set at 0.04 m/sec, just above the wall motion signals of the silicone tube, the reject was set at the minimum value, and the gain settings



Figure 3 Time interpolation procedure with the extraluminal method. A. Shows a tube with pulsatile flow and a flat flow velocity profile; arrows indicate flow direction. The 60-degree flow sector is updated from right to left as indicated by the arrow. P1 and P2 indicate the wall of the tube. B, Shows the velocity-time curve for three flow pulses. Numbers 1, 2, and 3 indicate the flow velocity maps obtained from sequential flow pulses. S1, S2, and S3 indicate the timing of the flow sweeps; S1 starts at the onset of the first flow pulse, S2 starts 20 msec after onset of the second flow pulse, and S3 starts 40 msec after onset of the third flow pulse. The duration of each flow sweep was 50 msec, and the dense parts of the flow pulses demonstrate the change in velocity during the flow sweep for each of the pulses. C, Shows the increase in the flow velocities that occurs during the sweep from position P1 to P2 recorded with a two-dimensional Doppler technique in pulsatile flow. Because the flow sector is updated from right to left, the first velocities appearing during each flow velocity map were located to the right in this panel. Numbers 1, 2, and 3 represent the records from pulse 1, 2, and 3, in panel B. D, Shows the time-corrected flow velocity profiles that can be obtained from the recorded flow velocities in panel C by time interpolation; in this example, at 50 msec from onset of flow in panel B. (Adapted from Samstad et al. Br Heart J 1989;62:177-84. Used with permission.)

were adjusted to give optimal quality of the spectral curve.

With the extraluminal method two-dimensional Doppler echocardiographic recordings were obJournal of the American Society of Echocardiography

tained with a CFM 700 (VingMed Sound), which is a combined two-dimensional echocardiographic, color, and conventional Doppler instrument. A combined imaging (7.0 MHz) and Doppler (6.0 MHz) transducer was used. The high-pass filter was set at 0.08 m/sec and, as with the intraluminal method. the reject was set at the minimum value and the gain settings were adjusted to give optimal quality of the recordings. The radial resolution was 0.4 mm, defined as the depth range of the flow sector divided by the number of samples in radial direction. Velocity data were resampled from three samples in radial direction, giving a resolution of 1.2 mm in radial direction from the transducer. Hence, the lateral resolution within the flow tube was 0.8 mm centrally in the tube and 0.7 mm laterally when corrected for the 45-degree angle between the transducer and the tube and the lateral deviation (30 degrees) from the centerline of the flow sector. Thus the effective axial resolution was proportional to the cosine between the ultrasound beam and the flow direction.

The lateral resolution within the tube, defined as a 50% decrease in backscattered signal from the central maximum, was less than 1 mm at the depth of recording with the intraluminal method and less than 1.5 mm with the extraluminal method at the depth of recording, which ranged from 2.8 cm centrally in the tube to 3.2 cm laterally in the tube.

**Recording procedures.** The technique of velocity recording with the intraluminal method has been described elsewhere.<sup>15</sup> The needle was inserted into the flowing medium at the desired diameter. Recordings were made of three flow cycles at each position before the transducer was positioned for the next velocity recording. This was done by moving the needle with the pulsed Doppler device along a ruler in steps of 2 mm across the tube from the distal wall of the tube until the transducer was withdrawn from the flow tube. The ruler was mounted perpendicular to the flow axis of the tube. Hence, the ultrasound beam was directed in parallel with the flow velocities during all recordings. All velocity recordings were stored as digital signals on videotape for later analysis.

With the extraluminal method serial time-gated flow velocity maps were recorded from the flow pulses. A trigger signal was generated by the flow simulator immediately before each flow pulse, and each flow velocity map was gated by this trigger signal. An increasing delay between the trigger pulse from the flow simulator and the onset of the timegated flow velocity map was made between each flow pulse. For each flow pulse, one flow velocity map was recorded. The first flow velocity map was started simultaneously with the onset of flow, and the following flow velocity maps were then incrementally delayed by 20 msec relative to the onset of the former (Figure 3). The combined tissue and twodimensional flow velocity recordings from each series of the sequentially delayed sweeps were transferred from the digital replay memory of the ultrasonograph to an external computer (Macintosh II, Apple Computer, Inc., Cupertino, California) immediately after the recording period with use of a commercial data program (TransDisp, VingMed Sound) by way of a commercial data port (NBDIO 24, National Instruments, Austin, Texas).<sup>18</sup>

### Protocol

The cardiovascular model was adjusted to produce peak flow velocities in the center of the tube of about 0.30, 0.50, and 0.70 m/sec, respectively. Inasmuch as both the intraluminal and the extraluminal methods were based on Doppler ultrasound, the recordings could not be done simultaneously because of interference between the two transducers. Recordings with the intraluminal method were done first and were followed by the extraluminal method at each of the three flow settings. With the extraluminal method the sweep time was varied: at peak flow velocity of 0.30 m/sec, it was set to 230 msec; at peak flow velocity of 0.70 m/sec, it was 80 msec. At peak flow of 0.50 m/sec recording was done twice, one with a sweep time setting of 230 msec and one with 80 msec, to investigate whether there were differences between the sweep time settings.

### Data Processing and Analysis

After the experiments the invasively recorded ultrasound signals were replayed on the Doppler instrument, and the spectral curves from the recorded flow cycles were printed out as hard copies on a thermic printer. The ultrasound signals recorded with the extraluminal method were analyzed with use of the digital velocity information from each recording stored in the computer. The postprocessing of all data was done independently by different investigators with regard to the two methods used.

With the intraluminal method the spectral curves of the recorded velocities from each position of the investigated diameter were digitized by hand on a graphic tablet (Tektronix 4957, Tektronix Inc., Beaverton, Oregon) interfaced to a computer (ND-500, Norsk Data, Oslo, Norway). The spectral curves were all narrow-banded and the mean velocities were



Figure 4 Spectral curve hard copy obtained with the intraluminal method at the flow setting with a maximum flow velocity of 0.5 m/sec. A narrow-band signal was obtained with the small sample volume.

traced and digitized by use of the second of the three spectral curves recorded at each position (Figure 4).

The digitized velocity information, 64 velocities from each curve, was then organized. The start of the flow cycle from each position was set equal in all recordings at each of the peak flow settings used. An array of digital velocity data from the points along the diameter was made at defined time intervals throughout the flow cycle. The data arrays were transferred to a standard text file for comparison with the extraluminal method.

With the extraluminal method the digital twodimensional Doppler ultrasound velocity information was analyzed by use of a dedicated computer program. Time interpolation between the velocity data from the sequentially gated maps was done on basis of the actual sweep time needed by the instrument to scan across the flow sector and the relative time increment from the onset of flow to the start each of the recorded flow maps (Figure 3). Velocities from the same diameter as that used with the intraluminal method were selected for analysis and velocities were calculated at steps of 2 mm across the tube. The flow velocities at each position were automatically corrected for the increment in angle from the centerline by the computer program, varying from 0 degrees to 30 degrees across the flow sector. The digital velocity data were then transferred to a standard text file for later comparison with the intraluminal method. All velocities recorded were also corrected for the 45-degree angle between the plane of the flow sector relative to the direction of the tube axis.

The structure of the text files containing velocity information was organized according to a standard procedure. The intervals between the measured velocity points was different from the two methods in both space and time. For comparison the values were



**Figure 5** Velocity data from recordings with a peak flow setting of 0.5 m/sec was analyzed as follows: **A**, Corrected flow velocity profiles obtained with the extraluminal method. **B**, Flow velocity profiles obtained with the intraluminal method. **C**, Average flow velocities at each position and time of flow obtained from the data in panels A and B. **D**, Scatterplot in which the differences between the two methods in A and B at each position and time are plotted along the y axis and the corresponding average velocities from panel C are plotted along the x axis. Limits of agreement between methods, that is, the mean difference  $\pm 2$  standard deviations, are indicated. **E**, A three-dimensional plot (as in panels A, B, and C) that shows the difference between the two methods in each position at each time of velocity calculation.

resampled at 2 mm increment in space and 20 msec increment in time at each position. The maximum deviation in spatial resolution between the two methods was thus 1 mm, and in time resolution the maximum deviation was 7 msec because with the intraluminal method the time resolution was 13 msec.

When comparing the two methods used, we restricted ourselves to study differences within the physical limits of either method. Flow may no longer be linear when it is close to the tube wall, and velocities recorded closer to the tube wall than 2 mm were excluded.

Because of the 45-degree angle between the flow sector plane with the extraluminal method and the direction of the flow within the tube and the angle of 30 degrees between the centerline and the lateral border of the flow sector, the high-pass filter limit of 0.08 m/sec was reached at velocities of 0.13 m/sec laterally in the tube. Accordingly, velocities at the start and at the end of each flow pulse were not compared when they were below the actual high-pass filter limit of 0.13 m/sec.

### Statistics

To compare the two methods statistically we used the method described by Bland and Altman.<sup>19</sup> The "true" velocity of each point across the diameter of the tube at each time was estimated as the average velocity of both methods at any given time of the actual flow pulse (shown in Figure 5, A, B, and C). For each setting of the flow simulator a mean value for the agreement between the two methods with regard to the obtained velocities was calculated (Figure 5, D).

|                                                 | Average of                | both methods               |                                         |                             |     |
|-------------------------------------------------|---------------------------|----------------------------|-----------------------------------------|-----------------------------|-----|
|                                                 | Peak velocity<br>(m/sec)* | Mean velocity<br>(m/sec)†‡ | Difference between<br>methods (m/sec)§‡ | CFM sweep<br>time<br>(msec) | n   |
| Color flow sector                               | 0.319                     | $0.227 \pm 0.071$          | $0.014 \pm 0.035$                       | 80                          | 198 |
| of 60 degrees                                   | 0.565                     | $0.375 \pm 0.102$          | $-0.010 \pm 0.050$                      | 230                         | 234 |
| C                                               | 0.710                     | $0.468 \pm 0.142$          | $-0.030 \pm 0.069$                      | 230                         | 234 |
| Color flow sector                               | 0.318                     | $0.227 \pm 0.055$          | $0.013 \pm 0.034$                       | 80                          | 115 |
| of 30 degrees                                   | 0.539                     | $0.385 \pm 0.010$          | $-0.010 \pm 0.035$                      | 230                         | 130 |
| U                                               | 0.700                     | $0.478 \pm 0.132$          | $-0.030 \pm 0.063$                      | 230                         | 130 |
| Comparison of 80<br>and 230 msec<br>sweep times | 0.536                     | $0.361 \pm 0.105$          | $-0.016 \pm 0.050$                      | 80,230                      | 234 |

**Table 1** Comparison of velocities obtained with the two ultrasound methods: with data from a color flow sectorof 60 degrees and 30 degrees and with the color flow method comparison of sweep times of 80 and 230 msec

n, Number of velocity data compared at each flow setting.

\*Maximum velocity obtained in the pulsatile flow at the actual flow setting.

†Mean velocity of average data from all positions throughout recording periods.

#Mean ± SD.

\$Mean difference between both methods when data from all positions thoughout the recording period were compared.

[Time used by the color Doppler instrument to update each flow velocity sector during recording.

The differences between the two methods were then calculated for each position and sample time throughout the recording periods, and a threedimensional plot was made to visualize the differences according to space and time (Figure 5, E).

The limits of agreement, that is, the mean difference with  $\pm$  two standard deviations (SD), were calculated from each recorded flow pulse. The difference in flow velocity obtained by the two methods at each position at the defined time intervals was also plotted against the average velocities obtained at the same points at the respective times of recording. Thus the magnitude of disagreement between the methods from the various flow settings could be quantitatively demonstrated as in the example in Figure 5, *D*.

Two sets of data were analyzed for each set of recordings. First, all velocity information from the tube model was analyzed at each velocity setting (color flow sector of 60 degrees), that is, a diameter of 18 mm. Second, only the velocities obtained from the central part of the tube were analyzed (color flow sector of 30 degrees) by neglecting the velocities obtained from the lateral 15 degrees of both sides of the color flow sector. These flow velocity profiles and the profiles obtained from the full sector were compared, and any differences in agreement between the methods were evaluated by use of the paired t test.<sup>20</sup>

Differences between the profiles obtained during

acceleration were compared with those obtained during deceleration from the respective flow settings by use of the paired t test.<sup>20</sup>

### RESULTS

The findings from the experiments are shown in Table 1. The differences between the two methods and the limits of agreement are visualized in the plots shown in Figures 6, 7, and 8.

At the flow settings studied the variation in mean flow velocity difference between the methods was small. These differences, as well as the standard deviation of the mean velocity differences, increased significantly with increasing peak flow velocity. The standard deviation of the difference between the methods as a percentage of the mean flow velocity of each setting ranged from 9% to 15%.

When the differences were compared between the methods with only the centrally located velocities (30-degree flow angle) versus all positions across the diameter of the flow tube (60-degree flow angle), no significant improvement in the agreement between the methods was found at any of the flow settings.

The largest difference between the methods was invariably found during the acceleration phase of the flow pulse, and the maximum difference increased



Difference between methods

**Figure 6** Comparison between data obtained with the intraluminal and extraluminal methods at a peak flow velocity setting of 0.3 m/sec. **A**, The average of both methods and the differences between them at each position and time are shown. The *horizontal lines* show the mean difference between methods and the limits of agreement, that is, the mean difference  $\pm 2$  standard deviations (n = 198). **B**, The difference in the flow velocity estimate between the two methods at each position and time is shown in a three-dimensional plot.

with increasing peak flow setting on the flow model, when also the flow acceleration increased. The largest differences in flow velocity between the methods (0.15 and -0.21 m/sec at the peak flow setting of 0.7 m/sec; 0.13 and -0.16 m/sec at the peak flow setting of 0.5 m/sec; and 0.11 and -0.11 m/sec at the peak flow setting of 0.3 m/sec) had a random localization with respect to position within the tube



Difference between methods

Figure 7 Comparison between data obtained with the intraluminal and extraluminal methods at a peak flow velocity setting of 0.5 m/sec. A, The average of both methods and the differences between them at each position and time are shown. The *horizontal lines* show the mean difference between methods and the limits of agreement, that is, the mean difference  $\pm 2$  standard deviations (n = 234). B, The difference in flow velocity estimate between the two methods at each position and time is shown in a three-dimensional plot.

and were nearly equally distributed with respect to the mean difference between the methods at the respective flow settings, as seen in Figures 6, 7, and 8. acceleration was  $4.8 \text{ m/sec}^2$  (mean,  $2.6 \text{ m/sec}^2$ ) and the maximum deceleration was  $-1.4 \text{ m/sec}^2$  (mean,  $-0.9 \text{ m/sec}^2$ ). At peak flow setting of 0.5 m/sec, the corresponding values for acceleration and de-

At peak flow setting of 0.3 m/sec the maximum



Difference between methods

**Figure 8** Comparison between data obtained with the intraluminal and extraluminal methods at a peak flow velocity setting of 0.7 m/sec. A, The average of both methods and the differences between them at each position and time are shown. The *horizontal lines* show the mean difference between methods and the limits of agreement, that is, the mean difference  $\pm 2$  standard deviations (n = 234). B, The difference in flow velocity estimate between the two methods at each position and time is shown in a three-dimensional plot.

celeration were 8.5 m/sec<sup>2</sup> (mean, 4.7 m/sec<sup>2</sup>) and -1.8 m/sec<sup>2</sup> (mean, -0.9 m/sec<sup>2</sup>) and at peak flow setting of 0.7 m/sec the respective values were 15 m/sec<sup>2</sup> (mean, 7.4 m/sec<sup>2</sup>) and -2.7 m/sec<sup>2</sup> (mean, -1.0 m/sec<sup>2</sup>). When separating the acceleration and deceleration phase the mean ( $\pm$  SD) differences at the peak flow setting of 0.3 m/sec were  $-0.01 \pm 0.04$  m/sec and  $-0.01 \pm 0.04$  m/sec, and at the peak flow setting of 0.7 m/sec the differences were

 $-0.05 \pm 0.08$  m/sec and  $-0.02 \pm 0.07$  m/sec during the acceleration and deceleration phases, respectively. The differences between acceleration and deceleration phases at peak flow settings of 0.3 m/sec and 0.7 m/sec were significant (p < 0.05), whereas at peak flow setting of 0.5 m/sec the difference between the two phases was not significant (p = 0.16).

With the extraluminal method a sweep time of 80 and 230 msec (Figure 9), a similar agreement be-

Volume 3 Number 6 November-December 1990



Difference between methods

Figure 9 Comparison of data obtained with the extraluminal method at a sweep time setting of 80 msec and 230 msec at a peak flow setting of 0.5 m/sec. A, The average of both sweep time settings and the differences between them at each position and time are shown, as well as the mean difference between the sweep time settings and the limits of agreement, that is, the mean difference  $\pm 2$  standard deviations (n = 234). B, The difference in flow velocity estimate between the sweep time settings is illustrated as a three-dimensional plot.

tween the setups was found as when the extraluminal and intraluminal methods were compared (Figure 9). The mean velocity difference with the extraluminal method at a sweep time of 80 and 230 msec was  $-0.016 \pm 0.050$  m/sec, whereas between the exuminal and the intraluminal methods it was  $-0.010 \pm 0.055$  m/sec at the same peak flow setting (p > 0.05).

### DISCUSSION

Our comparison between an intraluminal and an extraluminal method for plotting cross-sectional flow velocity profiles showed only small disagreement between the two methods. The mean velocity difference was less than  $\pm 0.03$  m/sec with peak flow settings ranging from 0.3 to 0.7 m/sec.

The increase in standard deviation of the mean difference between the two methods with increasing peak flow velocity was most likely attributable to the increased flow acceleration at the highest peak flow settings. The agreement between the two methods was less good during acceleration than during the deceleration phase in two of the three recording periods.

The observed differences between the two methods might be the result of a variety of factors influencing the individually obtained results for each method. The most obvious reason was probably that the two studies could not be done simultaneously because both methods were based on Doppler ultrasound technique and would interfere with each other if used simultaneously. Although the setting of the flow simulator was unchanged between recordings with the two methods, small variations in the flow velocities between flow pulses and between recording periods might have occurred. No systematic difference in the agreement between the cross-sectional flow velocity profiles obtained by the two methods was found with respect to the location within the tube. Hence, the two methods were regarded to be of equal validity with respect to the plotting of instantaneous cross-sectional flow velocity profiles.

Because no systematic error was found between the two methods used, the two different algorithms for estimating the velocity from the Doppler shift were considered to be of equal validity. The instrument with the intraluminal method used the Doppler spectrum analysis,<sup>21</sup> whereas the extraluminal method used an autocorrelation technique<sup>22</sup> for calculation of the flow velocities.

The flow within the tube was regarded to be rectilinear in axial direction and with a smoothly varying velocity profile. Hence, velocity gradients within the resolution volumes of both methods could be neglected.

# Possible Errors With the Resampling of Velocity Data

The velocity-time curves from the intraluminal recordings were resampled at 20 msec interval without interpolation. This gives a maximum time error of 7 msec, with a corresponding error in velocity estimate of 0.007 m/sec at an acceleration of 1 m/sec<sup>2</sup>. The maximum errors caused by the resampling of velocity data would be likely to appear in the recordings with a peak flow setting of 0.7 m/secwhere the highest accelerations and decelerations occurred, 15 m/sec<sup>2</sup> and -2.7 m/sec<sup>2</sup>, respectively. Hence a maximum error of 0.11 m/sec during acceleration and 0.02 m/sec during deceleration could be attributable to the resampling of the flow velocities before the comparison between the two methods.

### Possible Errors With the Intraluminal Method

With the manual digitizing of the spectral curves, exact timing of the start of the flow pulse at the different positions across the tube was another critical point. The variability attributable to the manual procedure was estimated to 5 m/sec from one position to the next, and this corresponds to an error of maximum 0.06 m/sec during acceleration and 0.01 m/sec during deceleration. The spectral curves obtained in this study were well defined with narrow-banded spectra (Figure 4). The estimated maximum error in the mean velocity attributable to the manual method was less than 0.10 m/sec.

With the intraluminal method no angle corrections were done because the ultrasound beam was directed upstream to the flow in parallel with the assumed direction of flow velocity.

### Possible Errors With the Extraluminal Method

With the extraluminal method the increments in the time delay of the start of the ultrasound sweep from onset of the flow and from one flow pulse to the other was controlled manually by increasing the delay period in fixed steps of 20 msec. The possibility of errors in the triggering procedure was checked by measuring the actual time intervals from the defined electrical trigger pulse on the flow simulator to the onset of each flow velocity map from hard copies made on each recorded flow map. The sweep times used for each flow velocity map in the different recording series were measured directly on the transducer controller within the ultrasonograph. The possibilities for incorrect time intervals between the flow velocity maps and in the duration of each map were thus regarded as small.

An error in correcting for the 45-degree angle between the flow velocity and the color flow sector plane of the extraluminal transducer would have introduced a systematic overestimation or underestimation of the velocities at all recording positions across the tube and at all points in time during the flow pulse. The effect of correcting for the angle between the centerline and the more lateral positions in the sector with the extraluminal method was studied by comparing a 30-degree sector with the full sector width of 60 degrees. However, no significant improvement in the agreement between the methods was found when comparing only the centrally located velocities. The overall errors with angle correction were considered to be small because the obtained difference in flow velocity between the two methods at the different flow settings was small.

The impact of the sweep time setting on the resulting flow velocity profiles with the extraluminal method was also studied. At long sweep time settings the time available for the sampling and calculation of data from each ultrasound beam within the flow sector was increased. However, differences in the velocities obtained with the two sweep time settings were within the same range as those obtained when the two different methods were compared.

### **Clinical Aspects**

Both methods presented in this study have been used for characterizing cross-sectional flow velocity profiles in vivo: the intraluminal in the ascending aorta and the extraluminal on mitral orifice.<sup>5,11</sup> The intraluminal method is inherently invasive and has been used only during operations, whereas the extraluminal method is noninvasive. Because the ultrasound Doppler technique with the invasive method is used in situ, an excellent lateral resolution is readily obtained. The extraluminal method is hampered by a lateral resolution that is not as good, because the distance from the ultrasound probe to the site of measurements usually also requires a lower ultrasound frequency than when the measurements are done in situ. In the clinical situation where the mitral flow was studied, a 3 MHz transducer was used and the depth of recording was 6 to 8 cm from the transducer. This setup gave lateral resolution of 2.1 to 2.5 mm, which was regarded as adequate for the purpose.11

The main problem with use of both methods in vivo is the need to have several flow pulses to obtain sufficient flow velocity information for constructing the cross-sectional flow velocity profiles. For this reason only patients with a regular heart rhythm are suitable. Movement of the transducer and the structures investigated may be another problem. These problems may be solved in part when several recordings are made and the changes in the flow pulses with respiration are corrected, as done with the invasive method,<sup>5</sup> or when the recordings are done during passive end-expiration, as done with the extraluminal method.<sup>11</sup>

Some of the disagreement in the present study

were probably caused by the resampling of velocity data for the purpose of comparison of the obtained cross-sectional flow velocity profiles. This type of error would not appear when either method is used alone.

### CONCLUSION

The agreement in flow velocities obtained with an intraluminal and an extraluminal method was good. This suggests that two-dimensional color Doppler ultrasound can be used to obtain flow velocity profiles across a flow channel if corrections are made for the sweep time and that cross-sectional flow velocity profiles can therefore be obtained noninvasively. The disagreements observed were most likely the result of minor inaccuracies in timing caused by the resampling of flow velocity data that was necessary for the comparison between the two methods. Small variations from one flow pulse to the other in the hydromechanical flow simulator may also to some extent have contributed to the variation between the methods.

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### 464 Samstad et al.

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# Paper III


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# Impact of changes in heart rate and stroke volume on the cross sectional flow velocity distribution of diastolic mitral blood flow

A study on 6 patients with pacemakers programmed at different heart rates

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# Abstract

The effect of changes in stroke volume on the cross sectional velocity distribution in the mitral orifice during passive mitral inflow was studied in six patients with total atrioventricular block, atrial fibrillation and VVI pacemakers during periods with different heart rates. The time velocity integrals recorded both in the left ventricular outflow tract and at the mitral orifice decreased significantly as the heart rate was increased from 60 to 80 and from 80 to 100 beats per minute.

Instantaneous cross sectional flow velocity profiles were constructed by time interpolation of the velocity data from each point in sequentially delayed two dimensional digital ultrasound maps. Each patient had a characteristic cross sectional flow velocity profile in the mitral orifice recorded at the level of the leaflet tips in a four chamber view. The velocity profiles varied between the patients. With increase in heart rate only minimal changes in the flow profiles from individual patients were seen.

The maximum velocity through the mitral orifice overestimated the cross sectional mean velocity at the same time by a factor of 1.4–1.9. The maximum time velocity integral overestimated the cross sectional mean by a factor of 1.4–1.8. The observed cross sectional skew varied between patients but did not change significantly with increasing heart rate and decrease in stroke volume.

#### Introduction

Noninvasive Doppler recording of flow velocity across the mitral valve has together with diameter measurements been used to estimate volume flow [1–5]. At the mitral orifice several approaches have been described using different levels of measurement. To obtain the velocity at the actual level pulsed Doppler with a limited sample volume has been used. A flat cross sectional flow velocity profile has been assumed, i.e. equal flow velocity distribution across the orifice. This has by some been based on lateral movement of the sample volume within the area of the mitral anulus [1], while others [2, 4] based their assumption on mitral flow velocity profiles obtained from invasive recordings using the pitot principle in dogs [6].

In a recent study using two-dimensional Doppler ultrasound technique, i.e. colour flow Doppler, the velocity profiles of early mitral flow in normal subjects showed a variable degree of skew [7].

The aim of the present study was to investigate the effect of varying heart rate and stroke volume on the cross sectional flow velocity profile in passive mitral blood flow in individual patients. Since changes in the early passive mitral flow might be compensated by changes in flow at atrial contraction only pacemaker dependent patients where no effective atrial contractions could be detected were included in the study.

# Patients and methods

Six patients, 3 males and 3 females, aged 58 to 83 years were included in the study (Table 1). All had atrial fibrillation as judged by the electrocardiograms recorded before and during the study period, and none had active atrial contractions resulting in mitral flow velocities at the Doppler examination.

None of the patients had evidence of mitral stenosis. All patients underwent a routine pacemaker control procedure before the onset of the study and the patients were included after informed consent.

The various pacemakers were all programmed in the VVI mode at heart rates of approximately 60, 80 and 100 beats per minute during the respective recording periods from each patient. To familiarize the patients with the recording procedure initial recordings were done at a heart rate of 70 beats per minute. These recordings were not used.

The Doppler ultrasound recordings were done with a VingMed CFM 700 (VingMed Sound, Oslo, Norway), a combined two-dimensional echo and colour Doppler ultrasound instrument with an additional accessible digital replay memory. A combined 3 MHz and 2.5 MHz transducer was used in all patients for two-dimensional echocardiogram and Doppler recordings respectively. During the two-dimensional (colour) Doppler recordings the high pass filter was set at 0.19 m/s, and the maximum recordable velocity was 1.8 m/s, that is twice the Nyquist frequency minus the high pass filter limit. The lateral resolution of the Doppler beam was less than 3 mm, defined as a 50% decrease in backscattered ultrasound signal from the centerline of the beam at a depth of 8 cm from the transducer when the flow sector angle was set to 30°.

In each patient a position with an optimal apical four chamber window to the mitral valve was used.

Following changes in the programmed heart rate a ten minute delay was used to obtain a steady state before recording.

At the various heart rates the velocities in the left ventricular outflow tract was first recorded using an apical window and pulsed Doppler with low or high pulse repetition frequency. The same position, i.e. where the highest velocities were obtained, was used at each heart rate. These recordings were made to detect relative changes in stroke volume. Tape recordings and hardcopies of the flow velocities were made for later analysis.

Secondly, serial time gated recordings of the mitral inflow were made using the colour flow mode. The flow maps were gated by the R-wave of the preceding QRS complex on the electrocardiogram, and the flow maps were delayed with 20 ms from one heart beat to the next. The recordings started before the onset of mitral inflow, continuing throughout diastole at all heart rates.

The sweep-time of the colour flow map varied between the patients from 54 ms to 65 ms, depending on the instrument setting with respect to the angle and the radial extension of the flow sector. The actual time periods used by the ultrasonograph to obtain each colour flow map were measured directly on the transducer controller of the instrument. No changes were made in the instrument setting between the different recordings in any of the patients.

| Table 1. Patient characteristi | cs. |
|--------------------------------|-----|
|--------------------------------|-----|

| Patient<br>number | Sex<br>M/F | Age<br>years | Duration of pacing years | Valvular status |
|-------------------|------------|--------------|--------------------------|-----------------|
| 1                 | М          | 76           | 2                        | Normal          |
| 2                 | F          | 83           | 9                        | Normal          |
| 3                 | F          | 66           | 2                        | MI+, Ao-valve   |
| 4                 | F          | 70           | 4                        | MI ++, AI +     |
| 5                 | М          | 74           | 0.5                      | Normal          |
| 6                 | М          | 58           | 3.5                      | AI++, Ao-valve  |
| Mean              |            | 71.2         | 3.5                      |                 |
| SD                |            | 8.6          | 3.0                      |                 |

Abbreviations: M; male, F; female.

MI + and MI ++; small and moderate mitral regurgitation respectively. AI + and AI ++; small and moderate aortic regurgitation respectively. Ao-valve; prosthetic aortic valve. Normal; no evidence of aortic or mitral regurgitation. After each recording the digital flow velocity and two-dimensional tissue data were transferred from the replay memory of the ultrasonograph to an external computer. The data transfer procedure has been described elsewhere [8]. In addition, the recordings were stored on videotape for later analysis of time intervals.

The described procedure was repeated at each programmed heart rate in all patients. All recordings were done during periods where the patients were asked to stop respiration in passive end-expiration, carefully avoiding the Valsalva manouvre.

# Data analysis

The flow velocity curves from the left ventricular outflow tract were manually digitized on a Hipad Digitizer (Model DT 11 H, Houston Instrument, Austin, Texas), and the time velocity integrals calculated by a personal computer using a custom made software. At each heart rate the time velocity

| 7 | able | 2.  |
|---|------|-----|
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integrals from four to six consecutive heart beats were averaged. These data were used to assess the change in stroke volume from one study period to the next (Table 2).

The digital velocity data from the mitral inflow obtained from the serially time-gated flow sweeps were postprocessed with a dedicated software (TransDisp, VingMed Sound, Oslo, Norway) on a personal computer (Macintosh II, Apple Computers Inc., Cupertino, California, USA).

The time delays from one flow map to the next as well as the sweep times for each flow map were known. Hence the skew in the recorded flow profiles introduced by the time necessary to record each flow sweep could be corrected for by time interpolation between the serially obtained flow maps as been described elsewhere [7,9]. A corrected flow velocity profile could therefore be obtained at any given time in the flow cycle. In this study corrected flow profiles were calculated with intervals of 20 ms, and the resulting cross sectional flow velocity profiles displayed either as an array of

| No. | Hr  | Ir Aorta TVI cm | Mitral    |            |           |            |      | Ratio |  |  |
|-----|-----|-----------------|-----------|------------|-----------|------------|------|-------|--|--|
|     |     |                 | MaxV cm/s | MeanV cm/s | MaxTVI cm | MeanTVI cm | Vel* | TVI   |  |  |
| 1   | 60  | 14.4            | 52        | 37         | 7.2       | 4.4        | 1.4  | 1.6   |  |  |
|     | 80  | 12.2            | 44        | 29         | 6.3       | 4.2        | 1.5  | 1.5   |  |  |
|     | 100 | 10.7            | 41        | 30         | 5.7       | 4.0        | 1.4  | 1.4   |  |  |
| 2   | 60  | 19.7            | 61        | 37         | 7.0       | 4.0        | 1.6  | 1.7   |  |  |
|     | 80  | 15.9            | 60        | 38         | 6.4       | 3.7        | 1.6  | 1.7   |  |  |
|     | 100 | 13.6            | 59        | 39         | 5.8       | 3.5        | 1.5  | 1.6   |  |  |
| 3   | 60  | 35.8            | 76        | 49         | 11.5      | 7.3        | 1.5  | 1.6   |  |  |
|     | 80  | 31.0            | 65        | 45         | 10.0      | 6.1        | 1.4  | 1.6   |  |  |
|     | 100 | 25.6            | 64        | 50         | 8.4       | 5.5        | 1.3  | 1.5   |  |  |
| 4   | 60  | 22.2            | 93        | 49         | 8.9       | 5.0        | 1.9  | 1.8   |  |  |
|     | 80  | 19.4            | 87        | 50         | 8.0       | 4.7        | 1.7  | 1.7   |  |  |
|     | 100 | 16.3            | 82        | 49         | 6.7       | 4.3        | 1.7  | 1.6   |  |  |
| 5   | 60  | 12.2            | 68        | 37         | 8.4       | 5.2        | 1.8  | 1.6   |  |  |
|     | 80  | 9.9             | 60        | 37         | 7.2       | 4.7        | 1.6  | 1.5   |  |  |
|     | 100 | 9.1             | 55        | 33         | 6.5       | 3.9        | 1.7  | 1.6   |  |  |
| 6   | 60  | 32.4            | 72        | 40         | 8.3       | 5.0        | 1.8  | 1.7   |  |  |
|     | 80  | 27.5            | 70        | 40         | 7.5       | 4.3        | 1.8  | 1.7   |  |  |
|     | 100 | 22.1            | 70        | 45         | 7.4       | 4.1        | 1.6  | 1.8   |  |  |

Abbreviations: No; patient number. HR; heart rate. TVI; systolic time velocity integral from the left ventricular outflow tract. MaxV; maximum velocity during mitral inflow. MeanV; mean cross sectional flow velocity at the time of MaxV. MaxTVI; maximum time velocity integral of mitral inflow. MeanTVI; mean cross sectional time velocity integral of mitral inflow. Ratio; ratio of maximum to mean values of MaxV to MeanV (Vel\*) and MaxTVI to MeanTVI (TVI).



*Fig. 1.* Three dimensional plots of the cross sectional flow velocity profiles obtained from two patients with increasing heart rate. The top panel shows the orientation of the axis of the plots. anterior; position of velocities along the anterior mitral leaflet posterior; position of velocities along the posterior leaflet Letters a, b and c refer to patient number 1 and letters d, e and f refer to patient number 5 in Tables 1 and 2 at heart rate 60, 80 and 100 beats per minute, respectively.

digital velocity data or as three-dimensional plots (Fig. 1). In all patients the level at the mitral leaflet tips was chosen for analysis.

The cross sectional flow velocity profiles were compared in three ways. First, the three-dimensional plots of the mitral inflow at the various heart rates were compared for each patient by visual inspection (Fig. 1). Secondly, the cross sectional flow velocity distribution at the time of peak flow was plotted separately at each heart rate (Fig. 2), and finally the time velocity integrals at the various



Fig. 2. Cross sectional velocity distribution at peak mitral flow at the different heart rates in each of the six patients.
Numbers 1–6 refer to the patient numbers in Tables 1 and 2.
Filled squares; heart rate 60 beats per min.
Open squares; heart rate 80 beats per min.
Filled diamonds; heart rate 100 beats per min.

positions across the valve orifice were compared at each heart rate (Fig. 3).

The maximum and the cross sectional mean velocity at the time of peak flow, and the maximum and the mean cross sectional time velocity integrals of the mitral flow were selected for comparison (Fig. 4–6). Also changes in the ratio of the maximum to the cross sectional mean velocity at peak flow, and of the time velocity integrals at the different heart rates were compared (Table 2).

# Statistics

The changes in the time velocity integrals from the left ventricular outflow tract and the mitral orifice (maximum and mean cross sectional time velocity integrals) from one recording period to the others

78



*Fig. 3.* Cross sectional distribution of time velocity integrals from early mitral flow in each patient at the different heart rates. Numbers 1–6 refer to the patient numbers in Tables 1 and 2. Filled squares; heart rate 60 beats per min. Open squares; heart rate 80 beats per min. Filled diamonds; heart rate 100 beats per min.

were calculated as per cent of the values obtained at the heart rate of 60 beats per minute. The range of observed changes with their mean values, standard deviation (SD) and the respective 95% confidence intervals were calculated [10]. The ratio of the maximum to the cross sectional mean values of the mitral flow velocities at the time of peak flow as well as the time velocity integrals of the mitral flow at the respective heart rates were compared by using the Bonferoni t-test [10].

# Results

With increase in the programmed heart rate from 60 to 80 and 100 beats per minute, a significant decrease in the time velocity integrals both in the left ventricular outflow tract and across the mitral



*Fig. 4.* Relative changes in the time velocity integral from the left ventricular outflow tract with increasing heart rate. All points are given as per cent of the time velocity integral at a heart rate of 60 beats per minute in each patient.

\* 95% confidence intervals for the relative change in the time velocity integral with increase in heart rate from 60 to 80 beats per minute. Mean decrease was 15.8% with 95% confidence intervals from 13.2% to 18.3%.

\*\* 95% confidence intervals for the relative change in time velocity integral with increase in heart rate from 80 to 100 beats per minute. Mean decrease was 12.6% with 95% confidence intervals from 8.9% to 16.0%.

valve was found in all patients as shown in the confidence interval plots in Figs 4–6.

The mitral flow velocity showed a decrease in the *maximum* time velocity integral ranging from 8.6 to 14.3% (mean  $11.3 \pm 2.2\%$ ) when the heart rate increased from 60 to 80 beats per minute, and a decrease of 1.2 to 16.2% (mean  $10.3 \pm 5.5\%$ ) at a heart rate increase from 80 to 100 beats per minute. With increase in heart rate from 60 to 100 beats per minute the decrease in the maximum time velocity integral ranged from 10.3 to 27.0% (mean  $20.5 \pm 6.0\%$ ).

The decrease in the mitral cross sectional *mean* time velocity integral ranged from 6.1 to 16.7% (mean  $9.7 \pm 4.1\%$ ) with the increase in heart rate from 60 to 80 beats per minute. The heart rate increase from 80 to 100 beats per minute showed a decrease ranging from 4.7 to 17% (mean  $8.4 \pm 4.7\%$ ), and with the change in heart rate from 60 to



*Fig. 5.* Relative changes in the maximum time velocity integral through the mitral orifice with increasing heart rate. All points are given as per cent of the time velocity integral at a heart rate of 60 beats per minute in each patient.

\* 95% confidence intervals for the relative change in the time velocity integral with increase in heart rate from 60 to 80 beats per minute. Mean decrease was 11.3% with 95% confidence intervals from 9.3% to 13.2%.

\*\* 95% confidence intervals for the relative change in the time velocity integral with increase in heart rate from 80 to 100 beats per minute. Mean decrease was 9.2% with 95% confidence intervals from 3.4% to 15.0%.

100 the decrease ranged from 8.6% to 25.2% with a mean of  $16.9\% \pm 6.5\%$ .

The flow velocity recorded with pulsed Doppler from the left ventricular outflow tract showed a decrease in the time velocity integral ranging from 6.6 to 16.7% (mean 12.4  $\pm$  3.7%) as the heart rate increased from 60 to 80 beats per minute. With an increase in heart rate from 80 to 100 beats per minute the decrease ranged from 8.1 to 19.7% (mean 14.7  $\pm$  4.1%), and with the change in heart rate from 60 to 100 beats per minute the decrease in time velocity integral ranged from 25.4 to 31.8% with a mean of 28.7%  $\pm$  2.7%.

The change in peak mitral flow velocity due to an increase in heart rate was variable (Table 2). With increase from 60 to 100 beats per minute, the corresponding relative decrease ranged from 3 to 21% (mean  $12.5\% \pm 8.0\%$ ). The corresponding changes in cross sectional mean flow velocities at the time of peak flow varied from an increase in mean flow



*Fig.* 6. Relative changes in cross sectional mean time velocity integral through the mitral orifice with increasing heart rate. All points are given as per cent of the time velocity integral at a heart rate of 60 beats per minute in each patient.

\* 95% confidence intervals for the relative change in time velocity integral with increase in heart rate from 60 to 80 beats per minute. Mean decrease was 9.7% with 95% confidence intervals from 6.0% to 13.5%.

\*\* 95% confidence intervals for the relative change in time velocity integral with increase in heart rate from 80 to 100 beats per minute. Mean decrease was 7.2% with 95% confidence intervals from 0.3% to 14.2%.

velocity of 5 cm/s to a decrease of 8 cm/s, mean relative decrease was 3% (± 11.8%).

The shape of the cross sectional flow velocity distribution at the time of peak flow varied between the patients (Fig. 2). In all patients except one the highest flow velocities were located closer to the anterior than to the posterior mitral leaflet. In one patient the highest flow velocities were located almost centrally in the mitral orifice. In the individual patients changes in heart rate did not result in any marked change in the position of the maximum flow velocity within the mitral orifice or in the flow velocity distribution across the orifice.

The ratio between the maximum velocity obtained and the corresponding cross sectional mean velocity ranged from 1.3 to 1.9 (mean  $1.6 \pm 0.17$ ). Changes in heart rate did not result in any systematic change in this ratio.

The relative position where the maximum flow velocity was recorded was nearly unchanged when

the various heart rates were compared in each patient (Fig. 2). A somewhat larger variation was seen in the relative positions of the maximum time velocity integrals when the cross sectional distribution in each patient at the different heart rates were compared (Fig. 3). The maximum time velocity integral was in nearly all recordings found more centrally in the mitral orifice than the corresponding maximum flow velocity.

The ratio between the maximum and cross sectional mean time velocity integrals ranged from 1.4 to 1.8 (mean  $1.62 \pm 0.11$ ). No systematic changes with changing heart rates were found (Table 2).

## Discussion

The visual impression of the three dimensional plots of the mitral flow is that both the skew and the shape of the instantaneous cross sectional flow velocity profiles varied between patients (Fig. 1). This is in agreement with earlier findings in normal subjects [7]. The increase in heart rate and associated decrease in stroke volume did not result in any marked change in the flow velocity profile in any of the subjects. Neither did the relative positions of the maximum velocity or the maximum time velocity integral change within the mitral orifice at the chosen level of recording (Figs 2, 3).

This visual impression was confirmed by the ratios of the maximum to the cross sectional mean velocities as well as of the cross sectional time velocity integrals (Table 2 and Figs 2 and 3). Although small variations were observed in individual subjects with increasing heart rate, no systematic or significant changes were observed between these ratios as the heart rate was increased from 60 to 80 and 100 beats per minute.

Assuming a constant area at the site of the velocity recording in the left ventricular outflow tract the decrease in systolic time velocity integrals showed a decrease in stroke volume with increasing heart rate. This finding is in agreement with other studies in patients treated with VVI pacemakers [11–13].

The decrease in the maximum and cross sectional mean time velocity integrals of the mitral flow with increasing heart rate was less consistent (Figs 5, 6). The difference between the changes in the velocity integrals from the left ventricular outflow tract and the mitral orifice was most likely due to changes in the effective flow areas at the two sites of velocity recording. In the outflow tract only minimal changes in the diameter would be expected, whereas at the mitral orifice the flow area may show a more marked change [14]. Another possible reason for the differences in time velocity integrals was the high pass filter setting at 19 cm/s with the colour flow technique. This might lead to an underestimation of the mitral time velocity integral at the lower heart rates since the longer duration of diastole could result in longer time periods with flow velocities below the high pass filter limit.

The largest discrepancy between changes in the time velocity integrals from the left ventricular outflow tract and the mitral orifice was found in the patient with a prosthetic aortic valve and a moderate paravalvular aortic regurgitation. In this patient the velocity integral in the left ventricular outflow tract decreased considerably more than at the mitral orifice. This might be due to a decrease in the regurgitant volume with the shorter diastole at higher heart rates [15]. In the patient with moderate mitral and mild aortic regurgitation the change in time velocity integrals was comparable to that in the other patients.

## Sources of error

Since the calculation of the cross sectional flow velocity profiles is based on interpolation between serially recorded flow maps, beat to beat variation in blood flow would give erroneous results. Also inaccuracies in the time interval from the R-wave of the electrocardiogram to the following colour flow map would introduce errors. Therefore the actual time intervals from all recordings were measured from hardcopies printed from the videorecordings made simultaneously with the two-dimensional Doppler data recordings. Another source of error could be introduced by thoracic movement and volume changes due to respiration. Hence the patients were asked to stop breathing in passive end expiration.

Changes in transducer position during the re-

cordings would introduce errors since no correction for the relative location of the Doppler sample areas was done in the postprocessing procedure, but relative changes from one beat to the next would easily be discovered since the two-dimensional tissue image was updated immediately before each flow sweep. However, minor changes in the nonvisualized azimuthal plane could occur without being discovered. Also small changes might occur between recording series in the same patient due to slight differences in the transducer position and in selection of Doppler sample areas during the postprocessing.

The actual movement of the mitral annulus during diastole was neglected since this normally cannot be corrected for with conventional pulsed Doppler recordings of mitral flow velocity.

#### Clinical implications

The results from this study as well as the findings reported from normal subjects [7] indicate a variable degree of skew of the flow velocity distribution at the mitral leaflet tips. The mean overestimation of the maximum time velocity integral from all recordings in the present study was 64% compared to the corresponding cross sectional mean time velocity integral. Although this comparison cannot be transferred directly to volume flow calculations it is a reminder of an important source of error when volume flow calculations are based on Doppler recordings from a small sample volume within the mitral orifice.

With increasing heart rate the individual variation of the ratio of the maximum to the cross sectional mean time velocity integral with increasing heart rate was within 15%, indicating only limited changes as the stroke volume decreased. However, these results were obtained in patients with nondilated ventricles, findings may differ in patients with a dilated left ventricle due to heart failure where changes in the mitral valve apparatus might influence the velocity distribution in the mitral orifice.

# Conclusions

Significant decreases were found in the left ventricular outflow tract and mitral time velocity integrals recorded with Doppler ultrasound as the heart rate was increased from 60 to 80 and from 80 to 100 beats per minute.

The cross sectional flow velocity profiles obtained from an apical four chamber view at the level of the mitral leaflet tips indicated a characteristic pattern in each patient. The flow velocity profile varied between the patients, whereas in the individual patient only minimal changes were found with the stroke volume changes associated with the increase in heart rate from 60 to 80 and from 80 to 100 beats per minute. The presence of valvular regurgitations in two of the patients did not influence this impression.

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# Paper IV



# Cross-sectional Early Mitral Flow-Velocity Profiles From Color Doppler in Patients With Mitral Valve Disease

Stein O. Samstad, MD; Ole Rossvoll, MD; Hans G. Torp; Terje Skjaerpe, MD, PhD; and Liv Hatle, MD

Background. Cross-sectional flow-velocity profiles from early mitral flow in 20 patients (10 with mitral regurgitation and 10 with mitral stenosis) were constructed from the velocity data from each point in sequentially delayed two-dimensional digital Doppler ultrasound maps.

Methods and Results. The data suggested that the early mitral flow studied in an apical four-chamber view was variably skewed in both patient groups. The maximum flow velocity overestimated the cross-sectional mean velocity at the same time by a factor of 1.12–1.86. The maximum time-velocity integral was 1.13–1.77-fold greater than the cross-sectional mean time-velocity integral. In patients with mitral regurgitation, the cross-sectional flow-velocity profile appeared to be most skewed at the level of the mitral leaflet tips. The level of the mitral annulus appeared to give the most homogenous flow-velocity distribution in both patient groups.

Conclusions. When calculations of volume flow are based on pulsed Doppler ultrasound recordings with a single sample volume, the possibility of a skewed flow-velocity profile must be taken into account. (Circulation 1992;86:748-755)

KEY WORDS • echocardiography, Doppler • mitral regurgitation • stenoses

he recording of mitral blood flow velocities has been used for cardiac stroke volume calculation<sup>1-5</sup> and for estimation of regurgitant fraction in patients with mitral regurgitation.<sup>6</sup> Various methods have been based on different ways of estimating flow area combined with pulsed wave Doppler ultrasound recordings. In some of the methods, a flat flow-velocity distribution across the mitral orifice has been assumed.<sup>1,2,4</sup> This assumption was made by Lewis et al1 based on lateral movement of the pulsed wave Doppler sample volume at the depth of area measurement; others<sup>2,4</sup> have based their assumption on a study by Taylor and Whamond7 in anesthetized dogs. Recently, a variably skewed flow-velocity distribution of the early mitral blood flow has been suggested from recordings obtained in normal subjects.8

The purpose of the present study was to obtain crosssectional flow-velocity profiles from the early mitral blood flow in patients with mitral valve disease using two-dimensional color Doppler ultrasound. Second, we wanted to study the individual variability in the obtained flow-velocity profiles both among patients with mitral regurgitation and among patients with mitral stenosis and to compare the findings from the two patient groups.

# Methods

#### Patients

Twenty patients -10 with moderate or severe mitral regurgitation (Table 1) and 10 with mitral stenosis (Table 2) – were included in the study after informed consent had been received. All patients were in sinus rhythm. Patient age ranged from 31 to 80 years, and mean patient age was  $63\pm10$  years for patients with pure mitral regurgitation and  $57\pm15$  years for patients with mitral stenosis.

Five of the patients with pure mitral regurgitation had prolapse of one mitral leaflet (anterior leaflet in patients 2, 3, and 9 and posterior leaflet in patients 4 and 8 [Table 1]). The other five patients in this group had dilation of the left ventricle with dilation of the mitral annulus as the most plausible reason for the mitral regurgitation. A mild but clinically insignificant aortic regurgitation was present in four patients, whereas none had aortic stenosis.

Five of the patients with mitral stenosis also had mild (n=3) or moderate (n=2) mitral regurgitation (Table 2). One of these patients had prolapse of the anterior mitral leaflet (patient 1 [Table 2]). Three patients had mild aortic regurgitation (patients 1, 9, and 10 [Table 2]), and one patient had mild aortic stenosis and moderate aortic regurgitation (patient 7 [Table 2]). Patients 2 and 5 (Table 2) had had mitral valve commissurotomy 7 and 19 years previously, respectively.

#### Doppler Echocardiography

The patients were positioned in a left semirecumbent position, and an apical four-chamber view to the mitral

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|         |       |    |       | Velocity | (cm/sec) |       |        | Time-velocity integral (cm) |         |       |  |
|---------|-------|----|-------|----------|----------|-------|--------|-----------------------------|---------|-------|--|
|         | Heart |    | Leaf  | let tips | Annulus  |       | Leafle | et tips                     | Annulus |       |  |
| Patient | (bpm) | MR | Max*  | Mean*    | Max*     | Mean* | Maxt   | Mean†                       | Max†    | Meant |  |
| 1       | 69    | 3  | 89    | 59       | 56       | 44    | 12.1   | 7.9                         | 7.8     | 5.5   |  |
| 2       | 62    | 3  | 98    | 58       | 68       | 55    | 8.9    | 6.1                         | 7.8     | 5.5   |  |
| 3       | 73    | 2  | 117   | 71       | 46       | 31    | 23.2   | 13.1                        | 12.0    | 8.3   |  |
| 4       | 77    | 3  | 131   | 79       | 106      | 57    | 17.9   | 10.9                        | 10.1    | 6.2   |  |
| 5       | 76    | 3  | 129   | 76       | 73       | 45    | 17.2   | 11.1                        | 8.5     | 6.4   |  |
| 6       | 83    | 2  | 101   | 67       | 88       | 61    | 12.0   | 8.6                         | 9.4     | 6.1   |  |
| 7       | 64    | 2  | 92    | 67       | 44       | 30    | 14.5   | 10.3                        | 7.1     | 6.3   |  |
| 8       | 81    | 3  | 114   | 83       | 69       | 50    | 16.9   | 11.9                        | 11.1    | 8.6   |  |
| 9       | 77    | 2  | 131   | 85       | 61       | 51    | 21.5   | 16.4                        | 14.3    | 11.2  |  |
| 10      | 73    | 2  | 121   | 69       | 72       | 55    | 12.0   | 7.8                         | 9.3     | 6.5   |  |
| Mean    | 73.5  |    | 112.3 | 71.4     | 68.3     | 47.9  | 15.6   | 10.4                        | 9.7     | 7.1   |  |
| SD      | 6.8   |    | 16.2  | 9.3      | 18.7     | 10.5  | 4.6    | 3.0                         | 2.2     | 1.8   |  |

TABLE 1. Maximum Flow Velocity and Time-Velocity Integral of Early Mitral Inflow Compared With the Simultaneous Mean Velocity and Mean Time-Velocity Integral Across the Mitral Orifice at the Level of the Leaflet Tips and the Annulus in Patients With Mitral Regurgitation

bpm, Beats per minute; MR, severity of mitral regurgitation: 1, mild; 2, moderate; 3, severe; \*max and mean, maximum velocity of the early mitral flow and cross-sectional mean velocity at the time of maximum velocity, respectively; †max and mean, time-velocity integral from the point in the flow sector giving the maximum value of early mitral flow and mean cross-sectional time-velocity integral of early mitral flow, respectively.

valve was used. The patients were asked to stop respiration in passive end expiration.

The recordings were made with a combined twodimensional echocardiographic and color Doppler ultrasonograph (VingMed CFM 700, VingMed Sound, Oslo, Norway). A combined imaging (3.0 MHz) and Doppler (2.5 MHz) transducer was used. The high-pass filter limit was set at 0.19 m/sec; the reject was set to the minimum value; and the gain settings were adjusted to provide optimal recording quality. The highest velocity that could be recorded with the two-dimensional Doppler technique was 180 cm/sec, i.e., twice the Nyquist frequency minus the high-pass filter limit. The radial resolution was 1.6 mm, defined as the depth range of the flow sector divided by the number of samples in radial direction. Velocity data were resampled from two samples in the radial direction, giving a resolution of 3.2 mm in radial direction from the transducer. The lateral resolution was 2.4-2.9 mm, defined as a 50% decrease in the backscatter signal from the central maximum at a depth of 8-10 cm from the transducer.

A routine echocardiographic and conventional Doppler ultrasound examination with grading of mitral regurgitation and stenosis was done. Mitral regurgitation was graded in a semiquantitative way from the impressions of the extent of the regurgitant flow in the left atrium combined with the intensity of the jet signal compared with that of forward flow and the width of the regur-

 TABLE 2.
 Maximum Flow Velocity and Time-Velocity Integral of Early Mitral Inflow Compared With the Simultaneous Mean Velocity

 and Mean Time-Velocity Integral Across the Mitral Orifice Near the Leaflet Tips and at the Annulus in Patients With Mitral Stenosis

|         |       | art                |    | Velocity (cm/sec) |       |      |         | Time-velocity integral (cm) |            |      |         |
|---------|-------|--------------------|----|-------------------|-------|------|---------|-----------------------------|------------|------|---------|
|         | Heart |                    | a  | At orifice        |       | An   | Annulus |                             | At orifice |      | Annulus |
| Patient | (bpm) | (cm <sup>2</sup> ) | MR | Max*              | Mean* | Max* | Mean*   | Max†                        | Mean†      | Max† | Mean†   |
| 1       | 79    | 1.5                | 2  | 112               | 90    | 48   | 36      | 18.3                        | 15.2       | 9.4  | 6.5     |
| 2       | 67    | 1.3                | 0  | 128               | 98    | 85   | 58      | 22.1                        | 19.0       | 9.8  | 7.8     |
| 3       | 61    | 1.6                | 0  | 84                | 55    | 43   | 31      | 20.0                        | 15.1       | 8.8  | 6.7     |
| 4       | 62    | 1.4                | 0  | 139               | 124   | 62   | 48      | 32.9                        | 26.8       | 15.9 | 11.8    |
| 5       | 72    | 1.1                | 1  | 87                | 56    | 63   | 42      | 19.2                        | 14.3       | 16.0 | 11.1    |
| 6       | 78    | 1.5                | 0  | 104               | 89    | 77   | 59      | 14.0                        | 11.1       | 14.1 | 11.2    |
| 7       | 66    | 1.1                | 0  | 88                | 72    | 60   | 42      | 23.4                        | 18.2       | 19.6 | 14.4    |
| 8       | 72    | 0.7                | 1  | 98                | 73    | 75   | 53      | 17.0                        | 13.9       | 16.0 | 12.8    |
| 9       | 70    | 1.6                | 1  | 130               | 99    | 90   | 72      | 20.0                        | 15.0       | 12.3 | 10.3    |
| 10      | 74    | 1.7                | 2  | 146               | 90    | 54   | 38      | 26.4                        | 16.3       | 9.0  | 6.3     |
| Mean    | 70.1  | 1.4                |    | 111.6             | 84.6  | 65.7 | 47.9    | 21.3                        | 16.5       | 13.1 | 9.9     |
| SD      | 6.1   | 0.3                |    | 22.9              | 21.1  | 15.6 | 12.6    | 5.3                         | 4.2        | 3.8  | 2.9     |

bpm, Beats per minute; area, estimated area of the stenotic mitral orifice; MR, grade of mitral regurgitation: 1, mild; 2, moderate; 3, severe; \*max and mean, maximum velocity of the early mitral flow and cross-sectional mean velocity at the time of maximum velocity at the defined level, respectively; †max and mean, time-velocity integral from the point in the flow sector giving the maximum value of early mitral flow and mean cross-sectional time-velocity integral of early mitral flow at the defined depth in the sector, respectively.

gitant jet at the orifice.<sup>9</sup> Mitral stenosis was graded according to the mean gradient and the pressure half-time obtained from maximum jet velocities.<sup>10</sup>

In the color flow mode, a series of two-dimensional flow maps was recorded from the early mitral inflow. Each flow map was time-gated by the preceding R wave of the simultaneously recorded ECG, and the time delay from the R wave to the start of the flow map was increased by 20 msec from one heartbeat to the next. The sweep time, i.e., the time required by the ultrasonograph to record each flow map, was set to 65 msec in all patients. Before each flow map was recorded, a twodimensional tissue image of the same plane was recorded. Therefore, one tissue map and one flow map were recorded from each heartbeat. The first tissue and flow maps were recorded at the start of the early mitral blood flow, and the recording period was terminated after onset of the atrial contraction with its increase in mitral flow velocity.

The combined tissue and two-dimensional flow-velocity recordings from each series of the sequentially delayed maps were transferred from the digital replay memory of the ultrasonograph to an external computer (Macintosh II, Apple Computer, Inc., Cupertino, Calif.) immediately after the recording period using a commercial data program (TRANSDISP, VingMed Sound, Oslo) and a commercial data port (NBDIO 24, National Instruments, Austin, Tex.).<sup>11</sup> In addition, each of the recording series was recorded on videotape for later measurement of time intervals.

The digital flow-velocity data from the early mitral flow period were postprocessed with the TRANSDISP program on the Macintosh computer. The duration of each flow map was known, as were the time delays from one flow map to the next relative to the preceding R wave of the ECG. Therefore, the skew of the recorded flow profiles caused by the sweep time necessary to record each flow map could be corrected for by time interpolation between the serially obtained flow maps. This procedure has been described in detail elsewhere.<sup>8.12</sup>

From the recorded flow maps, time-corrected crosssectional flow-velocity profiles could be constructed at any level of the mitral inflow with the computer software. In this study, profiles were constructed at 20-msec intervals throughout the early mitral flow period, and the velocities were calculated for each 2 mm across the flow channel. In each patient group, two levels were chosen for further analysis. In the patients with mitral regurgitation, the levels at the mitral annulus and at the leaflet tips were analyzed. In the patients with mitral stenosis, the velocity profiles at the mitral annulus and at a level near the stenotic orifice were analyzed. The position near the orifice was chosen 3-5 mm upstream from where the flow velocity reached a velocity twice the Nyquist frequency. All cross-sectional flow-velocity profiles were traced perpendicular to the assumed direction of blood flow. The levels of flow-velocity profile calculation were selected at the time of peak flow.

The time-corrected cross-sectional flow-velocity profiles from each patient were displayed as either threedimensional plots (Figures 1 and 2) or data arrays suitable for further analysis. At each level in the mitral flow channel, the ratio of the maximum flow velocity to the cross-sectional mean velocity at the time of peak flow was calculated, as was the relative position within the orifice of the maximum flow velocity in each patient (Figures 3 and 4). In addition, the time-velocity integral from each position across the flow channel was calculated to obtain the ratio of the maximum to the crosssectional mean time-velocity integral and the relative position of the maximum value within the orifice (Figures 5 and 6).

#### Statistical Analysis

Results are given as ranges and sample mean values (SD) from each of the two patient groups, and where suitable, results from the two groups were compared using the Bonferroni t test.<sup>13</sup>

#### Results

The results were plotted as cross-sectional flowvelocity profiles versus time to provide a three-dimensional impression of the flow-velocity distribution with time. The largest variability in the flow-velocity distribution was found at the level of the mitral leaflet tips in the patients with mitral regurgitation. In these patients, the flow-velocity profile at the leaflet tips ranged from clearly skewed with the highest velocities located close to either the anterior or the posterior mitral leaflet to a nearly parabolic shape with the highest velocities almost central in the orifice (Figures 1A and 1C). At the level of the mitral annulus (Figures 1B and 1D), the flowvelocity distribution appeared to be flatter, but some variation between the patients remained. In patients with mitral stenosis (Figure 2), the cross-sectional flowvelocity distribution appeared to be more homogenous than in the patients with mitral regurgitation, except in patient 10, who had combined moderate mitral regurgitation and stenosis (Table 2).

#### Cross-sectional Flow-Velocity Profiles at Peak Flow

The difference between the maximum and the crosssectional mean velocities ranged from 10 cm/sec at the level of the mitral annulus in patient 9 (Table 1) to 56 cm/sec at the level near the stenotic orifice in patient 10 (Table 2). Mean differences were  $20\pm11.7$  cm/sec and  $41\pm10.3$  cm/sec at the level of the annulus and at the mitral leaflet tips in the patients with mitral regurgitation, respectively. In patients with mitral stenosis, mean differences were  $18\pm4.7$  cm/sec and  $27\pm12.1$  cm/sec at the annulus and at the level near the stenotic orifice, respectively.

At the time of peak mitral flow, the ratios of the maximum to the cross-sectional mean flow velocity in patients with mitral regurgitation ranged from 1.2 to 1.86 with a mean value of  $1.43\pm0.2$  at the annulus and from 1.37 to 1.75 with a mean of  $1.58\pm0.13$  at the leaflet tips (Figure 3A). In the patients with mitral stenosis, this ratio ranged from 1.25 to 1.5 with a mean of  $1.38\pm0.08$  at the annulus and from 1.12 to 1.62 with a mean of  $1.34\pm0.17$  at the level near the stenotic orifice (Figure 4A).

Figures 3 and 4 show the ratios of the maximum to the cross-sectional mean velocity and the relative locations of the maximum velocity within the mitral orifice at the two levels of measurement in both the patients with mitral regurgitation and those with mitral stenosis.



FIGURE 1. Plots of instantaneous early mitral flow-velocity profiles against time in two patients with mitral regurgitation. Axis scaling and orientation are shown at top. Plots a and b are from patient 4 (Table 1), and plots c and d are from patient 9. Left panels: Plots a and c are recorded at the level of the mitral leaflet tips. Right panels: Plots b and d are recorded at the level of the annulus.

# Cross-sectional Distribution of the Time–Velocity Integrals

The difference between the maximum time-velocity integral and the cross-sectional mean time-velocity integral from the same time period ranged from 1 cm at the level of the mitral annulus in patient 7 (Table 1) to 10 cm at the level near the stenotic orifice in patient 10 (Table 2). The mean differences between the maximum and the cross-sectional mean time-velocity integrals were  $2.7\pm0.9$  cm and  $5.2\pm2.1$  cm at the annulus and at the level of the leaflet tips in the patients with mitral regurgitation, respectively. The respective differences in the patients with mitral stenosis were  $3.2\pm1.2$  cm at the annulus and  $4.8\pm2.2$  cm at the level near the stenotic orifice.

The maximum time-velocity integrals overestimated the cross-sectional mean time-velocity integral at all sites of recording in both patient groups. In the patients with mitral regurgitation, the maximum overestimated the mean cross-sectional time-velocity integral with a ratio ranging from 1.13 to 1.63 and a mean of  $1.39\pm0.14$ at the annulus and a ratio ranging from 1.31 to 1.77 and a mean of  $1.5\pm0.13$  at the level of the leaflet tips. In patients with mitral stenosis, the same ratio ranged from 1.19 to 1.45 with a mean of  $1.3\pm0.09$  at the mitral annulus and from 1.16 to 1.62 with a mean of  $1.3\pm0.13$ at the level near the stenotic orifice.

The ratios of the maximum to the mean crosssectional time-velocity integrals and the relative location of the maximum time-velocity integrals at the two levels of recording are shown for each patient in Figures 5 (mitral regurgitation) and 6 (mitral stenosis). Heart rate ranged from 62 to 83 beats per minute (mean,  $73.5\pm6.8$  beats per minute) in the patients with mitral regurgitation (Table 1) and from 61 to 79 beats per minute (mean,  $70.1\pm6.1$  beats per minute) in the patients with mitral stenosis.

#### Discussion

The data indicate that the flow-velocity distribution across the mitral orifice varies among patients with mitral regurgitation as well as patients with mitral stenosis. In patients with mitral regurgitation, the most uniform flow-velocity distribution was seen at the level of the mitral annulus. At the orifice, the profile was more skewed, as indicated in Figure 1. In patients with mitral stenosis, the velocity distributions were more similar both at the annulus and at a level near the stenotic orifice and the velocity profile did not appear to become more skewed closer to the orifice (Figure 2).

#### Cross-sectional Flow-Velocity Distribution at Peak Flow

The maximum velocity versus the simultaneous mean cross-sectional flow velocity gives an indication of the skewness of the flow-velocity profile at the time of peak flow. The maximum velocity overestimated the crosssectional mean flow velocity by a factor of 1.12–1.86 at peak flow, indicating a considerable variation among the 20 patients examined. No significant differences between the level of the annulus and the level at or near the mitral leaflet tips were found within any of the patient groups. However, in patients with mitral regurgitation, the mean





ratio obtained at the level of the mitral leaflet tips was significantly different from the ratios obtained both at the level of the mitral annulus and at the level near the mitral orifice in patients with mitral stenosis (p < 0.05).

# Cross-sectional Distribution of the Time–Velocity Integral

In volume-flow calculations, the time-velocity integral obtained from pulsed Doppler recordings is multiplied with the flow area. In the present study, the time-velocity integrals were calculated at each point across the mitral orifice. The maximum versus the mean cross-sectional time-velocity integral gives an impression of the possible errors in volume-flow calculation depending on the sample volume position during the velocity recording. The maximum overestimated the cross-sectional mean time-velocity integral by a factor of 1.19-1.77 in the 20 patients studied. Within each of the patient groups, there were no significant differences between the obtained ratios at the two levels of recording. The mean ratio obtained at the level of the mitral leaflet tips in the patients with mitral regurgitation was significantly larger than the ratios obtained both near the stenotic orifice and at the annulus in patients with mitral stenosis (p < 0.05).

# Location of Maximum Velocity and Maximum Time–Velocity Integral

As expected from the variability among patients in the cross-sectional flow-velocity distribution with time (Figures 1 and 2), a wide variation in the relative locations of the maximum velocities and the maximum time-velocity integrals was found (Figures 3-6). In the



FIGURE 3. Information on patients with mitral regurgitation. Numbers refer to patients (Table 1). Panel a: Plot of ratio of maximum velocity to mean cross-sectional flow velocity at the time of maximum velocity of early mitral flow at the leaflet tips (solid bars) and at the annulus (patterned bars). Panel b: Site of maximum velocity within the mitral orifice is shown for each patient at the level of the mitral leaflet tips (solid diamonds) and at the annulus (patterned diamonds). Leaflet margins are indicated as solid vertical lines.



FIGURE 4. Information on patients with mitral stenosis. Numbers refer to patients (Table 2). Panel a: Plot of ratio of maximum velocity to mean cross-sectional flow velocity at the time of maximum velocity of early mitral flow at the level near the stenotic orifice (solid bars) and at the annulus (patterned bars). Panel b: Site of maximum velocity within the mitral orifice is shown for each patient at the level near the stenotic orifice (solid diamonds) and at the annulus (patterned diamonds). Leaflet margins are indicated as solid vertical lines.

five patients with mitral regurgitation due to mitral valve prolapse, the highest velocities as well as the maximum time-velocity integrals at the orifice were found on the contralateral side of the prolapsing valve (n=4) or on the ipsilateral side (n=1). This might be due to the direction of the regurgitant jet following the atrial wall around the cavity of the left atrium during systole and possibly contributing to an increased velocity on either of the two sides of the mitral flow channel during diastole. In the other patients, the regurgitant jets were not directed to either of the sides of the left atrium. These patients showed no definite pattern regarding where the maximum values were recorded-not at the levels of the mitral annulus or close to the orifice of mitral valve. This finding was in contrast to a similar study on normal subjects in which the highest velocities usually were found closer to the anterior than to the posterior leaflet.8 The maximum time-velocity integrals appeared to be located slightly more centrally than the respective maximum velocities in both the patients with mitral regurgitation and those with mitral stenosis.

#### Clinical Implications

The finding of a variably skewed velocity distribution of mitral blood flow may have clinical implications. Volume flow calculations from pulsed wave Doppler recordings may be critically hampered by the lack of information about velocities outside the Doppler sample area when the cross-sectional flow-velocity distribution is highly skewed or parabolic. In addition, the



FIGURE 5. Information on patients with mitral regurgitation. Numbers refer to patients (Table 1). Panel a: Plot of ratio of maximum time-velocity integral to mean cross-sectional timevelocity integral of early mitral flow at the level of the leaflet tips (solid bars) and at the annulus (patterned bars). Panel b: Site of maximum time-velocity integral within the mitral orifice is shown for each subject at the level of the leaflet tips (solid diamonds) and at the level of the annulus (patterned diamonds). Leaflet margins are indicated by solid vertical lines.

relative location of the maximum time-velocity integrals had variable locations within the mitral orifice in patients with mitral regurgitation. For the purpose of volume flow calculations, the level of the mitral annulus appears to be more suitable since the flow-velocity distribution was more homogenous at this location.

In patients with mitral stenosis, the flow-velocity distribution appeared to be more uniform than that in those with mitral regurgitation except for patient 10, who had combined mild mitral stenosis and moderate mitral regurgitation (Table 2). However, variations in the relative location of the maximum velocity as well as in the maximum time-velocity integral within the orifice were also found in this patient group. The finding of a relatively flat flow-velocity profile at the level of the mitral annulus makes this location more suitable for volume flow calculations and thus for calculations of the stenotic flow area based on the continuity equation.

In the present study, no correction for the diastolic movement of the mitral annulus in the longitudinal direction of the heart was made because this usually cannot be done when recordings are made with regular pulsed Doppler ultrasound. Thus, the effective flow area at the two levels of recording was subjected to changes due not only to the blood flow but also to relative movement of the anatomic structures during the recording period.

## Study Limitations

The main limitation of the present study was that the cross-sectional flow-velocity profiles were obtained



FIGURE 6. Information on patients with mitral stenosis. Numbers refer to patients (Table 2). Panel a: Plot of ratio of maximum time-velocity integral to mean cross-sectional time-velocity integral of early mitral flow at a level near the stenotic orifice (solid bars) and at the annulus (patterned bars). Panel b: Site of maximum time-velocity integral within the mitral orifice is shown for each subject at a level near the stenotic orifice (solid diamonds) and at the level of the annulus (patterned diamonds). Leaflet margins are indicated by solid vertical lines.

from only one plane and one time sequence from each patient. However, the plane selected for this study is the commonly used two-dimensional plane for orientation in combination with conventional pulsed and continuous wave Doppler recordings. Series of recordings made sequentially while rotating the transducer between each recording period would eliminate this limitation, but the procedure would have been very time consuming with the present instrumentation and software.

The lateral resolution of each transmitted ultrasound beam with the transducer frequency used caused two neighboring points (at 2-mm intervals) to overlap at a position where the power of the backscattered signals was reduced to 55-65% of the central maximum of each beam. The influence of points that were further apart was not significant, and the resolution was regarded as appropriate for the study.

The high-pass filter limit was set to 19 cm/sec in all recordings, and velocities under this limit could not be recorded. Therefore, velocities at the very start of flow were lost, but this error was regarded as small. The maximum velocity was limited by the Nyquist frequency, but through adjustment of the baseline during analysis with the TRANSDISP program, the effective maximum velocity from each recording was 180 cm/sec with a depth setting of the flow sector of 14 cm from the transducer. This upper velocity limit was below the maximum value of the velocities recordable from the

stenotic orifice in some of the patients with mitral stenosis. Velocity recordings from the orifice would be aliased in these patients and thus less suitable for analysis with the present software. For this reason, a level 3–5 mm upstream from the stenotic orifice was chosen for analysis in this patient group. With appropriate alterations of the computer software, the higher velocities from the jet in mitral stenosis could be recorded, but this was not applied in the present study because of limited experience with this technique.

#### Sources of Error

The time interpolation procedure used to compensate for the distortion of the recorded cross-sectional flow-velocity profiles due to the time required for the ultrasonograph to update the two-dimensional flow sector necessitated series of heartbeats with only minor changes in the flow pattern and RR intervals. Therefore, only patients with regular sinus rhythm were chosen for inclusion in the study.

Respiratory changes of volume flow through the mitral valves are likely to occur as is intrathoracic movement of the heart with respiration. Because the two-dimensional tissue images of the heart were made immediately before each flow map, the location of the mitral valve could easily be recognized throughout each recording period and changes resulting from transducer or thoracic movement could be discovered.

Possible errors due to the angle between blood flow and the ultrasound beam were compensated for in the plane of the flow sector of the instrument. This was done by an angle-correction algorithm within the TRANSDISP software with the assumption that the levels chosen for analysis in the mitral flow channel were drawn perpendicular to the assumed direction of blood flow. Errors due to the angle between direction of the blood flow and the direction of the ultrasound beam in the nonvisualized azimuthal plane could not be corrected for. However, a mismatch of up to 15° would give an error of the estimated flow velocity of less than 6% of the actual velocity.

#### Other Methods

For the study of flow-velocity distribution across heart valves and large vessels, several methods have been used. Whamond and Taylor<sup>7</sup> used an invasive method based on the Pitot principle in the study of mitral flow-velocity distribution in the canine. Others have used hot film anemometri<sup>14</sup> or pulsed Doppler technique<sup>15,16</sup> for the study of aortic flow-velocity profiles.

Noninvasive methods have also been used for the study of left ventricular outflow tract and aortic flow-velocity distribution. The magnetic resonance technique used by Nayler et al<sup>17</sup> and Klipstein et al<sup>18</sup> allows multiplane visualization, but the method is hampered by the lack of velocity calibration. The multigate pulsed Doppler technique used by Jenni et al<sup>19,20</sup> gives excellent spatial and time resolution but is hampered by the angle of incidence necessary to obtain recordable velocities. Color flow imaging with an analog flow display technique has been used to visualize the blood flow events of the left ventricle.<sup>21</sup> The velocity resolution of this technique was limited to eight steps (colors) of 6.75 cm/sec in each flow direction, and the recordings were

done during several heartbeats. No correction for the distortion of the flow-velocity profiles introduced by the sweep time was done.

#### Conclusions

The results of the present study provide new information on the distribution of early mitral flow velocity across the mitral valve at a level close to or at the orifice and at the annulus in patients with mitral valve disease. The instantaneous flow-velocity profiles obtained from an apical four-chamber view were variably skewed at both levels in both the patients with mitral regurgitation and those with mitral stenosis. The possibility of a skewed flow-velocity distribution should be borne in mind when recordings from a small area in the valve orifice are used for volume flow calculations.

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# Interobserver and Intraobserver Variation of Cross Sectional Early Mitral Flow Velocity Profiles from Color Doppler

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# ABSTRACT

Cross sectional velocity profiles from early mitral blood flow were constructed from the velocity data obtained from sequentially delayed two-dimensional digital Doppler ultrasound maps in ten normal subjects. The data suggested that the early mitral flow studied from an apical four chamber view was variably skewed between subjects. The maximum flow velocity overestimated the cross sectional mean velocity at the same time by a factor of 1.2 to 1.7. The maximum time velocity integral from early mitral inflow was 1.3 to 1.9 times higher than the cross sectional mean time velocity integral. Based on three sets of recordings made by two observers the inter- and intraobserver variation of both the analyzing and the recording procedures of the method were studied. The limits of agreement were within 27% defined as percent of the sample mean for the intraobserver comparisons and within 35% for the interobserver comparisons respectively. The obtained results indicate that the method is reliable. The presence of a variably skewed cross sectional flow velocity distribution of the early mitral flow should be kept in mind when flow velocity measurements are made from only a part of the flow area for the purpose of volume flow calculations.

# **INTRODUCTION**

**R** ecently a new method based on two-dimensional (color) Doppler ultrasound was introduced to obtain instantaneous cross sectional flow velocity profiles from early mitral inflow. In ten normal subjects these cross sectional flow velocity profiles were shown to be variably skewed when an apical four chamber view to the mitral valve was used.<sup>(1)</sup> The method has shown good agreement with an invasive method on cross sectional flow velocity distribution in an in vitro pulsatile flow model.<sup>(2)</sup>

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# SAMSTAD ET AL.

An earlier inter- and intraobserver variability study from mitral flow velocity recordings based on conventional pulsed Doppler ultrasound recordings has reported variable agreement between observers.<sup>(3)</sup> The purpose of this study was to investigate the inter- and intraobserver variability of the measurement of the cross sectional flow velocity distribution from early mitral blood flow in healthy subjects.

# PATIENTS AND METHODS

Ten normal subjects, 4 males and 6 females aged 22 to 25 years (mean  $23 \pm 1.1$  years) were included in the study after informed consent. None of the subjects had clinical, electrocardiographic, or echocardiographic evidence of heart disease, and all were in regular sinus rhythm. During recording the subjects were lying in a left lateral position and the ultrasound transducer was placed in the apical area with a four chamber view to the mitral valve.

The ultrasound measurements were taken with a VingMed CFM 700 (VingMed Sound, Oslo, Norway), a combined two-dimensional tissue imaging and Doppler ultrasound instrument. A combined 3 MHz and 2.5 MHz annular array transducer was used for two-dimensional tissue imaging and the color flow mapping respectively. Each two-dimensional Doppler flow velocity map (color flow map) was constructed from color coded digital velocity information from 64 sample volumes along 64 sequentially transmitted ultrasound beams in each flow map. The two-dimensional flow map was recorded immediately after the recording of the two-dimensional tissue map.

In the color flow mode the high pass filter was set at 0.19 m/s, with the depth settings used in the study the Nyquist frequency was 1.0 m/s. The lateral resolution of each Doppler ultrasound beam at a depth of 8 cm from the transducer was 3 mm, defined as a 50% decrease in the backscattered signal from the center line of the beam. A fixed instrument set-up with a flow sector width of 30° was used during all recordings. With the actual instrument set-up the time needed for updating each flow map was 65 ms as measured from the transducer controller of the instrument.

The recordings for the time corrected cross sectional flow velocity profiles were started before the onset of the early mitral flow. Each flow map was gated by the R-wave of the electrocardiogram and each new flow map was incrementally delayed relative to the preceding R-wave with 20 ms by an automatic processor within the ultrasonograph. One color flow map was recorded from each heart beam throughout the recording period which was terminated after the onset of blood flow due to atrial contraction. During the recording periods the subjects were asked to stop breathing in passive end-expiration, carefully avoiding the Valsalva maneuver. Each subject underwent three recording procedures. First one investigator (A) made one recording, then the second investigator (B) made one and the first investigator (A) made the last recording. This procedure was followed in all subjects, and the investigators were not aware of each other's recordings.

After recording, the two-dimensional tissue and flow velocity data were transferred from the digital replay memory of the ultrasound instrument to an external computer (Macintosh II, Apple computers Inc., Cupertino, CA) for later analysis. This procedure has been described in detail elsewhere.<sup>(4)</sup> The data were blinded before further analysis.

The digital data were analyzed on the computer using a commercial computer program (TransDisp, VingMed Sound, Oslo, Norway). The time lag needed by the ultrasound instrument to update a flow map introduces an artificial skew in the cross sectional flow profile in a pulsatile flow. Therefore a dedicated computer program was used for time interpolation between sequentially delayed flow maps. The sweep time needed for updating the flow maps was 65 ms during all recording series. Hence the same algorithm was used during the postprocessing of all recordings.

With the use of the time interpolation algorithm a time corrected two-dimensional flow velocity color flow map was displayed by the computer. These color flow maps were used for analysis of the cross sectional flow velocity distribution from each recording series. Depending on the heart rate 8 to 12 time corrected flow velocity maps were constructed from each set of recordings.

The instantaneous cross sectional flow velocity profiles were measured at the level of the mitral leaflet tips at the time of maximum opening of the valve. The cross sectional line along which the velocities were acquired was parallel with the mitral annulus. The same cross sectional level was used throughout each recording period for all cross sectional flow profiles. The calculated cross sectional flow velocity profiles were displayed as two-dimensional line plots and as digital velocity data from each 2 mm along the selected diameter. The digital velocity data were transferred to a data text file for subsequent inter- and intraobserver comparison and for construction of three dimensional plots of the cross sectional flow velocity distribution against time (Figure 1).

For the inter- and intraobserver comparison the following variables were used. The velocity at peak early mitral flow and the cross sectional mean velocity at the same time were calculated as well as the ratio



FIG. 1. Three-dimensional plots of the cross sectional flow velocity profiles obtained from subject number eight in Tables 1 to 4. The top right panel shows the orientation of the axis of the plots. I) and II); two sets of blinded flow velocity data analyzed by observer A from recordings made by observer B. III); blinded flow velocity data analyzed by observer B from recordings made by observer B. IV) and V); blinded flow velocity data analyzed by observer A from two different sets of recordings made by observer A.

# SAMSTAD ET AL.

between the two. Likewise the maximum and the cross sectional mean time integrals were calculated from each recording period and the ratio between the two was estimated. The selected variables were compared for inter- and intraobserver variation of the analyzing procedure and for the combination of recording and analysis procedures.

To study intraobserver variability of the analyzing procedure one set of recordings from each subject was analyzed twice by one observer (A), and one of these analyzed data sets was compared to the analyzed data from the second observer (B) to study the interobserver variability. All data files were blinded before analysis.

Finally, the combined variability of recording and analysis was studied. Blinded analyses from two separate sets of recording by observer A were compared to study the intraobserver variability, and the set of blinded data recorded and analyzed by observer B was compared to one of the data sets obtained by observer A to study the interobserver variability. After unblinding the data arrays from each subject were matched with respect to the duration of early mitral inflow before the comparison of the time velocity integrals.

# STATISTICS

Results are given as ranges and sample means  $\pm$  the standard deviation. For inter- and intraobserver studies the method described by Bland and Altman was used by calculating the mean difference and the standard deviation of that difference between two data sets.<sup>(5)</sup> The sample means and standard errors of the variables from each data set as well as the mean differences with the respective standard errors from each comparison were tested with t-test adjusted for multiple comparison by the Bonferroni method.<sup>(6)</sup>

# RESULTS

The three-dimensional plots of the cross sectional flow velocity distribution against time allowed a visual comparison of the results of the analysis of the same velocity data by two observers (Figure 1 panels I, II, and III) as well as the results from analyzing separate recordings (Figure 1 panels III, IV, and V). A wide range of variation in velocity distribution between the different subjects was seen. The cross sectional flow velocity profile ranged from skewed with the highest velocities located towards the anterior mitral leaflet to nearly parabolic shaped profiles with the highest velocities located more centrally in the mitral orifice.

At the time of peak early mitral flow the maximum velocity ranged from 53 to 98 cm/s (mean 72 cm/s  $\pm$  10.7 cm/s) (Table 1) and the cross sectional mean velocity at the same time ranged from 36 to 72 cm/s (mean 51.9 cm/s  $\pm$  9 cm/s) (Table 2). The ratio of the maximum to the cross sectional mean velocity at the time of peak flow ranged from 1.17 to 1.7 with a mean ratio of 1.4 ( $\pm$ 0.13) (Figure 2).

The maximum time velocity integral from early mitral flow ranged from 6.1 to 12.4 cm (mean 9.3 cm  $\pm$  1.6 cm) (Table 3) and the cross sectional mean time velocity integral ranged from 3.8 to 8.1 cm with a mean of 6 cm ( $\pm$ 1 cm) (Table 4). The ratio of the maximum to the cross sectional mean time velocity integrals from early mitral flow ranged from 1.3 to 1.9 (mean 1.5  $\pm$  0.14) (Figure 3).

The inter- and intraobserver variation with regard to the maximum and cross sectional mean velocities at the time of peak flow were small when the same set of recordings were analyzed (Table 5). The limits of agreement (Figure 4), were within 20% of the respective mean estimates for the whole study group. When all recordings were analyzed separately by the respective observers the limits of agreement were wider. The limits of agreement for the maximum velocity at peak flow and mean cross sectional flow velocity were within 35% (interobserver variation) and 16% and 27% (intraobserver variation) of the respective sample means. The limits of agreement regarding the ratio of the maximum to the cross sectional mean velocity at the time of peak flow were all 20% or less of the sample mean values for all intra- and interobserver comparisons.

The intra- and interobserver variations as regards the limits of agreement of the variables from the time velocity integrals of the early mitral flow were within 20% and 26% of the sample means for the maximum and cross sectional mean time velocity integrals (Table 6). For the ratio between the two variables the limits of agreement was less than 21% of the sample means.

| Subject | - 1  | II   | 111  | IV   | V    |
|---------|------|------|------|------|------|
| 1       | 71   | 76   | 69   | 76   | 71   |
| 2       | 62   | 65   | 60   | 73   | 77   |
| 3       | 69   | 67   | 70   | 60   | 58   |
| 4       | 83   | 78   | 74   | 84   | 80   |
| 5       | 76   | 76   | 74   | 72   | 71   |
| 6       | 66   | 69   | 64   | 69   | 66   |
| 7       | 86   | 95   | 93   | 85   | 83   |
| 8       | 65   | 68   | 62   | 65   | 62   |
| 9       | 80   | 93   | 98   | 72   | 85   |
| 10      | 53   | 56   | 56   | 58   | 62   |
| mean    | 71.2 | 74.3 | 72.1 | 71.4 | 71.3 |
| SD      | 10.3 | 12.3 | 13.8 | 9.0  | 9.5  |

TABLE 1. MAXIMUM VELOCITY OF EARLY MITRAL BLOOD FLOW (CM/S)

Subject; subject number. I and II; two sets of blinded flow velocity data analyzed by observer A from recordings made by observer B. III; blinded flow velocity data analyzed by observer B from recordings made by observer B. IV and V; blinded flow velocity data analyzed by observer A from two different sets of recordings made by observer A.

None of the sets of variables studied showed significant differences with respect to the various inter- or intraobserver analyses performed.

# DISCUSSION

The flow velocity variables of early mitral flow obtained in this study were comparable to earlier published data<sup>(1)</sup> as regards the mean values of the maximum and cross sectional mean velocities at peak flow as well as the maximum and mean cross sectional time velocity integrals. As in the former study, a wide variation in the

|         |      | FLOW | (CM/S) |       |      |
|---------|------|------|--------|-------|------|
| Subject | 1    | 11   | 111    | IV    | V    |
| 1       | 43   | 49   | 42     | 45    | 51   |
| 2       | 50   | 53   | 49     | 56    | 56   |
| 3       | 52   | 54   | 54     | 42    | 47   |
| 4       | 62   | 61   | 59     | 72    | 63   |
| 5       | 56   | 52   | 54     | 48    | 49   |
| 6       | 47   | 50   | 46     | 50    | 47   |
| 7       | 64   | 71   | 71     | 70    | 61   |
| 8       | 49   | 46   | 45     | 45    | 43   |
| 9       | 57   | 55   | 61     | 46    | 59   |
| 10      | 36   | 38   | 39     | 38    | 40   |
| mean    | 51.6 | 52.7 | 52.0   | 51.21 | 51.7 |
| SD      | 8.7  | 8.7  | 9.9    | 11.5  | 7.9  |
|         |      |      |        |       |      |

 TABLE 2.
 MEAN CROSS SECTIONAL VELOCITY OF EARLY MITRAL BLOOD

 FLOW (CM/S)
 FLOW (CM/S)

Subject number. I and II; two sets of blinded flow velocity data analyzed by observer A from recordings made by observer B. III; blinded flow velocity data analyzed by observer B from recordings made by observer B. IV and V; blinded flow velocity data analyzed by observer A from two different sets of recordings made by observer A.

# SAMSTAD ET AL.



FIG. 2. Ratio of the maximum to the mean cross sectional flow velocity at the time of peak flow. Roman letters I to IV in the upper panel denote the order of analyses and recordings as in Tables 1 and 2. Arabic numbers indicate the subject numbers.

cross sectional flow velocity distribution between individual subjects was found. However, the ratios of both the maximum/cross sectional mean velocity at peak flow, and the maximum/mean cross sectional time velocity integrals varied less in the present study.

The maximum and the cross sectional mean velocity at peak flow showed the widest range of the limits of agreement. The narrowest limits of agreement were found for the ratios of the maximum to the cross sectional mean velocity at peak flow and the maximum to the cross sectional mean time velocity integrals.

When complete sets of velocity recording and data analysis made by observer A and B were compared, the widest limits of agreement were observed. However, the mean differences showed no systematic nor significant difference from the other modes of comparison.

The variation in blood flow in each subject from one recording to the next was considered to be small since the time between each recording was less than 30 minutes and the subjects were at rest in the recumbent position both during and between recordings.

| Subject | 1    | 11   | 111  | IV   | V    |
|---------|------|------|------|------|------|
| 1       | 11.4 | 12.4 | 11.8 | 11.3 | 10.4 |
| 2       | 9.8  | 9.3  | 9.8  | 10.4 | 11.2 |
| 3       | 8.2  | 7.4  | 8.2  | 8.6  | 8.0  |
| 4       | 7.0  | 8.1  | 9.8  | 9.4  | 9.9  |
| 5       | 7.7  | 7.7  | 8.1  | 8.9  | 9.0  |
| 6       | 9.9  | 10.3 | 10.2 | 10.4 | 9.5  |
| 7       | 9.0  | 8.6  | 8.0  | 7.3  | 7.0  |
| 8       | 10.5 | 10.4 | 10.3 | 10.0 | 10.3 |
| 9       | 11.3 | 11.5 | 12.0 | 10.3 | 11.1 |
| 10      | 6.1  | 6.5  | 6.6  | 7.1  | 7.5  |
| mean    | 9.07 | 9.21 | 9,47 | 9.38 | 9.38 |
| SD      | 1.81 | 1.91 | 1.72 | 1.39 | 1.4  |

| TABLE 3. | MAXIMUM | Тіме | VELOCITY | INTEGRAL | OF | EARLY | MITRAL |
|----------|---------|------|----------|----------|----|-------|--------|
|          |         | BLO  | OD FLOW  | (СМ)     |    |       |        |

Subject; subject number. I and II; two sets of blinded flow velocity data analyzed by observer A from recordings made by observer B. III; blinded flow velocity data analyzed by observer B from recordings made by observer B. IV and V; blinded flow velocity data analyzed by observer A from two different sets or recordings made by observer A.

| Subject | I    | 11   | 111  | IV   | V    |
|---------|------|------|------|------|------|
| ]       | 7.1  | 8.1  | 7.3  | 7.4  | 6.6  |
| 2       | 7.3  | 6.5  | 7.6  | 7.8  | 8.1  |
| 3       | 6.0  | 5.7  | 6.1  | 6.0  | 5.5  |
| 4       | 5.0  | 5.9  | 5.9  | 6.6  | 6.5  |
| 5       | 4.6  | 4.7  | 5.1  | 5.5  | 5.5  |
| 6       | 5.9  | 6.0  | 5.6  | 6.5  | 6.2  |
| 7       | 6.2  | 5.9  | 5.8  | 5.0  | 4.5  |
| 8       | 6.5  | 6.7  | 6.4  | 6.8  | 6.6  |
| 9       | 6.1  | 6.6  | 7.1  | 5.4  | 6.3  |
| 10      | 3.8  | 4.2  | 4.3  | 4.7  | 4.8  |
| mean    | 5.84 | 6.02 | 6.11 | 6.17 | 6.07 |
| SD      | 1.08 | 1.09 | 1.02 | 1.03 | 1.02 |

 
 TABLE 4.
 MEAN CROSS SECTIONAL TIME VELOCITY INTEGRAL OF EARLY MITRAL BLOOD FLOW (CM)

Subject; subject number. I and II; two sets of blinded flow velocity data analyzed by observer A from recordings made by observer B. III; blinded flow velocity data analyzed by observer B from recordings made by observer B. IV and V; blinded flow velocity data analyzed by observer A from two different sets of recordings made by observer A.

# Differences in recording

Minor differences in transducer position, rotation, and angling probably occurred between separate recordings. Such variations probably were the cause of the wider limits of agreement found when complete sets of velocity recording and data analysis were compared.

The use of the color flow maps are in general hampered by a rather crude velocity resolution. The color coding of velocities is usually based on eight different color codes in each direction. With the high pass filter set at 0.19 m/s and a Nyquist limit of 1 m/s the velocity resolution was approximately 0.1 m/s when the velocities were displayed as colors. The different hues of each color indicate the intensity of the signal, and does not aid in improving velocity resolution. Hence only limited help from the color flow maps could be expected with respect to the aiming of the transducer in order to obtain optimum reproducibility from one recording to the other.





| Comparison of maxi  | mum velocities at peak flov | v (cm/s)             |
|---------------------|-----------------------------|----------------------|
| Comparison          | Sample mean                 | Mean difference (SD) |
| I versus II         | 72.7                        | -3.1 (± 5.25)        |
| II versus III       | 73.2                        | 3.8 (± 4.64)         |
| III versus IV       | 71.7                        | $0.7 (\pm 11.54)$    |
| IV versus V         | 71.3                        | 0.1 (± 5.47)         |
| Comparison of cross | sectional mean velocities   | at peak flow (cm/s)  |
| Comparison          | Sample mean                 | Mean difference (SD) |
| I versus II         | 52.2                        | -1.2 (± 3.70)        |
| II versus III       | 52.4                        | $0.7 (\pm 3.64)$     |
| III versus IV       | 51.6                        | $0.8 (\pm 8.54)$     |
| 117                 |                             |                      |

TABLE 5. COMPARISON OF VARIABLES OBTAINED AT PEAK EARLY MITRAL FLOW

Comparison of the ratios of the maximum to the

cross sectional mean velocity at peak flow

| Comparison    | Sample mean | Mean difference (SD) |
|---------------|-------------|----------------------|
| I versus II   | 1.4         | $-0.03 (\pm 0.13)$   |
| II versus III | 1.4         | $0.02 (\pm 0.06)$    |
| III versus IV | 1.4         | $-0.03 (\pm 0.09)$   |
| IV versus V   | 1.4         | $0.04 (\pm 0.13)$    |

I versus II; Intraobserver variation of analysis from the same recordings. II versus III; Interobserver variation of analysis from the same recordings. III versus IV; Interobserver variation of analysis and recording made from the same subjects. IV versus V; Intraobserver variation of analysis and recording made from the same subjects.

The transfer of the digital tissue and flow velocity data should not introduce errors in the flow velocity recordings. Neither was there any likelihood that errors from the algorithms used by the TransDisp program could occur since the same settings with respect to lateral and radial resolution, time interpolation, and signal power threshold were used during all analyses by both observers.

The influence of surrounding structures and blood flow on the flow maps of early mitral flow could not be estimated. However, signals recorded by side lobes are theoretical sources of errors that might interfere with the true flow velocity estimates.

## Differences in analysis

With the TransDisp software analyses from each recording could be done several times with different approaches to the recorded flow velocity data. A defined program set-up was used for all analyses and differences due to different program settings were not likely to occur. The analyses were based on the visual impression of the time corrected flow velocity maps in relation to the imaged tissue structures. By definition the cross sectional flow velocity distribution was obtained from a line across the mitral orifice at the level of the anterior mitral tip at peak flow parallel to the mitral annulus. Since the time of peak flow could be difficult to define from the color flow map alone due to its rather crude velocity resolution, the chosen time of the assumed peak flow might have varied slightly. This could have led to small differences in the level within the mitral orifice from where the cross sectional flow velocities were obtained from one analysis to the other.

Differences in the chosen level at the mitral orifice was observed as differences of the width of the effective flow area. A difference up to 4 mm was seen between analyses made from the same recordings at

# TIME CORRECTED CROSS SECTIONAL FLOW VELOCITY PROFILES



**FIG. 4.** Scatterplot obtained from the maximum flow velocity at peak early mitral inflow as obtained from two blinded sets of analyses by observer A from one set of recordings made by observer B (Table 1, columns I and II). Differences between the velocity data from each subject as obtained from the two sets of analyses are plotted along the y-axis and the respective mean velocities from each subject are plotted along the x-axis.

| Comparison of maximum velocity integrals (cm) |                                |                    |  |  |
|-----------------------------------------------|--------------------------------|--------------------|--|--|
| Comparison                                    | Sample mean                    | Mean difference    |  |  |
| I versus II                                   | 9.1                            | $-0.13 (\pm 0.64)$ |  |  |
| II versus III                                 | 9.3                            | $-0.27 (\pm 0.72)$ |  |  |
| III versus IV                                 | 9.4                            | $0.1 \ (\pm 0.75)$ |  |  |
| IV versus V                                   | 9.4                            | $0 (\pm 0.65)$     |  |  |
| Comparison of cross.                          | sectional mean time velocity i | integrals (cm)     |  |  |
| Comparison                                    | Sample mean                    | Mean difference    |  |  |
| I versus II                                   | 5.9                            | $-0.18 (\pm 0.56)$ |  |  |
| II versus III                                 | 6.1                            | $-0.09(\pm 0.56)$  |  |  |
| III versus IV                                 | 6.1                            | $-0.06 (\pm 0.77)$ |  |  |

 TABLE 6.
 COMPARISON OF VARIABLES OBTAINED FROM TIME VELOCITY

 INTEGRALS OF EARLY MITRAL FLOW

Comparison of the ratios of the maximum to the cross sectional mean time velocity integral

IV versus V

| Comparison    | Sample mean | Mean difference    |
|---------------|-------------|--------------------|
| I versus II   | 1.5         | $0.03 (\pm 0.07)$  |
| II versus III | 1.5         | $-0.03 (\pm 0.12)$ |
| III versus IV | 1.5         | $0.03 (\pm 0.15)$  |
| IV versus V   | 1.5         | $-0.02 (\pm 0.08)$ |

6.1

 $0.11 (\pm 0.51)$ 

I versus II; Intraobserver variation of analysis from the same recordings. II versus III; Interobserver variation of analysis from the same recordings. III versus IV; Interobserver variation of analysis and recording made from the same subjects. IV versus V; Intraobserver variation of analysis and recording made from the same subjects.

# SAMSTAD ET AL.

two occasions. These differences of the assumed cross sections increase the differences in the cross sectional mean velocity and time velocity integrals.

A low signal-to-noise ratio would introduce loss of flow velocities depending on the high pass filter and signal power threshold setting. Loss of velocities occurred at points with no colors displayed within the respective color flow maps and were most likely to occur along the mitral leaflet tips at times of low flow velocities. These variations were likely to introduce increased variability in all comparisons since these points were not necessarily equally included during analysis of the respective recordings.

#### Other studies

In another study, the same method for time interpolation of flow velocity data obtained from color flow mapping was compared to an invasive Doppler method in an in vitro hydromechanical model.<sup>(2)</sup> The limits of agreement in that case ranged from 20% to 30% when the two methods were compared throughout a whole flow cycle. The limits of agreement were calculated as percent of the mean velocity from 115 to 130 different velocity data points in time and location.

In vivo the present method has been used for blood flow velocity recordings in the left ventricular outflow tract and in the aortic and mitral orifices. Rossvoll et al. reported a coefficient of variation of 11% for the beat to beat variation of velocity coordinates recorded at the aortic anulus.<sup>(7)</sup> Wiseth et al. reported intraobserver repeatability betwen series of recording of 9.4% and 11.8% for the maximum and mean velocity at peak flow from recordings obtained from the left ventricular outflow tract.<sup>(8)</sup> The repeatability was calculated as the absolute difference between repeated analyses in percent of the mean value. Another study from the left ventricular outflow tract reported coefficients of variation ranging from 18% to 23% when all single pixel velocity determinations from two series of recording after one another were compared.<sup>(9)</sup>

In the mitral valve position no studies on the reproducbility of the present method have been done previously. However, with the use of pulsed Doppler ultrasound technique a study of the reproducibility of the mitral flow velocity has been reported.<sup>(3)</sup> In that study narrower limits of agreement for the inter- and intraobserver comparison for peak velocity were found. This might be a function of the different method used. Recordings within the mitral orifice were guided by the highest velocities obtained from continuous wave Doppler recording and not by the tissue imaging as in the present study. During recording the pulsed Doppler mode was used. The sample volume of the equipment (2 MHz single transducer, SD 100, VingMed Sound) had a lateral resolution of 5.2 mm to 6.5 mm at depths of 8 to 10 cm from the transducer and presumptively the default setting of the instrument was used with a radial resolution of 4 mm. Thus a considerably larger sample volume was used and some degree of smoothing of the obtained spectral curves was likely to occur compared to the smaller sample volume used in the present study.

## Limitations of the study

For the study of inter- and intraobserver variations a cross sectional flow velocity profile from only one level in one plane was used. Rotating the transducer and obtaining velocity profiles from several planes would have given more complete information on the velocity distribution, but this procedure would have been very time consuming with the present instrumentation and software.

Excluding mitral blood flow due to atrial contraction introduces another limitation. However, experience has shown that the inclusion of the active flow phase would require the patient to stop breathing for an unconfortably long time period.

The high pass filter was set at 0.19 m/s. Velocities at the start of mitral flow and in the later part of the early flow were therefore lost. At peak flow the impact of the high pass filter limit was probably limited, also at the very beginning of flow where the increase in flow velocity was very steep.

The difference in duration of the recorded flow periods from each subject varied from 0 to 40 ms between individual recordings. Where differences in duration between recordings occured these were always located in the later parts of the early filling period. However, the duration of the longer recording series was equalized to the shortest series from each subject for the comparison of the time velocity integrals. This was done to give a better estimate of differences due to the method and not due to the duration of each recording series.

# TIME CORRECTED CROSS SECTIONAL FLOW VELOCITY PROFILES

The short time span between the two recordings by one observer might have introduced some bias with respect to location of the transducer and the position of the subject during recordings. However, the blinding procedure after the recording probably reduced the effect of bias introduced during recording. The use of a standard instrument set-up with regard to the sweep time and the high pass filter setting reduced the variability between the respective recordings from each subject.

# Sources of error

A regular heart rhythm was critical as the method used to compensate for the distortion of the recorded flow velocity maps was based on time interpolation requiring series of heart beats with only minor changes in the flow pattern and R-R-intervals. Hence only subjects with regular sinus rhythm was chosen for the study.

With respiration small changes in volume flow through the mitral orifice as well as intrathoracic movement of the heart might occur. To omit these problems the subjects were asked to stop breathing in passive end expiration during recording. Changes in transducer position during each recording series would be discovered from the tissue images updated immediately before the recording of the respective color flow maps from each heart beat.

The TransDisp program automatically corrected for angle distortions regarding the flow direction within the plane of the flow sector. This was done by an algorithm assuming the blood flow to be perpendicular in positive or negative direction relative to the line drawn across the flow area. Errors due to the angle between the direction of blood flow and the direction of the ultrasound beam in the nonvisualized azimuthal plane could not be corrected for. However, a mismatch of up to 15° would given an error of the flow velocity estimate of less than 6% of the actual velocity.

# CONCLUSIONS

The time corrected cross sectional flow velocity profiles obtained from an apical four chamber view in ten normal subjects were variably skewed. Inter- and intraobserver comparison of the flow velocity data showed good agreement for the analyzing and the recording procedure used. The widest limits of agreement were found with the interobserver comparison of complete sets of velocity recording and analysis from each subject. The limits of agreement between the ratios of the maximum to the cross sectional mean flow velocities at the time of peak flow and between the maximum and mean time velocity integrals were less than 20%. The presence of variably skewed cross sectional flow velocity profiles should be kept in mind when volume flow calculations are made from one sample volume within the mitral blood flow.

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