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A laser Doppler catheter for monitoring both phasic and mean coronary vein flow

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Summary. A new catheter-type laser Doppler velocimeter has been developed to monitor coronary vein flow. A thin graded-index multimode optical fiber (outer diameter of 125 μm) is set inside a 5-F catheter, and eight elastic silicon rubber spikes are arranged radially toward the vessel wall to fix the catheter tip in or near the axial region of the coronary vein. He-Ne laser light (wave length = 632.8nm) is introduced into the blood through the optical fiber, and reflected light is collected by the same fiber. The Doppler signal is detected by a spectrum analyzer. To avoid any effect by the spikes on flow, the fiber is extended from the catheter tip by 3 mm at the time of measurement. Straight and curved tubing was used to examine the accuracy of flow measurement. The flow velocities recorded by the catheter, which were measured by an electromagnetic flowmeter, exhibited excellent linearity (r = straight: 0.982, curved: 0.996). The blood flow velocity in the great cardiac vein was measured by this method in five dogs. The predominantly systolic waveform, which is a characteristic of the coronary vein flow, was observed in all of the dogs. The great cardiac vein velocity increased around the beginning of the ventricular ejection and decreased gradually after the peak formation at mid- or end-diastole. In addition to this main peak, small flow components were frequently observed during isovolumic contraction and the atrial contraction phase, although these flow components varied in individual dogs. Following left anterior descending artery occlusion, the great cardiac vein flow velocity decreased significantly. Following reopening of the left anterior descending artery, the great cardiac vein flow velocity increased, showing a reactive hyperemic response, and then it returned to the control level. In conclusion, our catheter-type laser Doppler velocimeter holds promise for continuous monitoring of both mean and pulsatile coronary vein flow velocities in man.

Key words: Optical fiber-coronary catheter – Coronary vein flow velocity – Coronary flow reserve

The monitoring of coronary vein blood flow has been used as a measure of myocardial blood perfusion in man. It is an important indicator of coronary flow reserve, and a useful monitor of medical interventions. Current coronary vein flow measurement techniques include thermodilution [1], inert-gas diffusion [2], ultrasonic Doppler flowmetry [3] and the fiber optic liquid crystal catheter [4]. Laser Doppler velocimetry is considered to be a powerful technique capable of measuring blood flow velocity accurately in a small sample volume [5–9]. However, until recently the application of this method was restricted because of the relatively low transparency of both blood and the vessel wall to laser light. Tanaka and Benedek were the first to use a fiber-optical catheter to introduce laser light into a blood vessel using a relatively large diameter fiber (outer diameter: 500 μm) [10]. However, their method was unable to detect instantaneous change in pulsatile blood flow, and to differentiate reverse from forward flow.

In order to apply the laser Doppler velocimeter

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to real-time observation of phasic blood flow velocity, we developed a laser Doppler velocimeter using an optical fiber [11–14]. The fiber delivers light into a vessel and collects the scattered light from the moving erythrocytes through the same fiber. Using this system, we have made physiological measurements of coronary artery and vein velocities in dogs [15–17]. Kilpatrick also developed a laser Doppler velocimeter with an optical fiber and demonstrated its utility for blood flow velocity measurements in the coronary vein [18, 19]. With clinical application of the laser Doppler catheter in mind, it is most crucial to keep the fiber tip (velocity sensor) near the axial region of the vessel. This is because of a decrease in the velocity signal in regions near the vessel wall, although the velocity profile across the coronary vein has been reported to be relatively flat [19, 20]. In our laser Doppler velocimeter, eight elastic silicon rubber spikes are arranged around the catheter, with each spike pointing radially towards the vessel wall to fix the fiber tip in or near the axial region. This rubber spike holder also prevents deformation of the coronary vein during the cardiac cycle, and thus keeps its diameter relatively constant. Our laser Doppler catheter has the following potential advantages over the conventional methods: (1) high spatial resolution, (2) a thin optical probe with a low thrombogenic potential, (3) absence of electrical interference, and (4) the ability to measure both phasic blood flow velocity and mean velocity over long periods of time.

Materials and methods

Optical arrangement of the laser Doppler velocimeter with an optical fiber

The principle and optical arrangements of our system have been described in our previous publications [11–14]. In brief, a linearly polarized He-Ne laser beam (frequency: f_0, wave length: 632.8nm) is divided into incident and reference beams by a beam splitter (Fig. 1). The incident beam is focused onto the entrance of an optical fiber using an objective microscope lens and is delivered directly into the blood flow from a flat termination of the fiber inserted into the vessel. The light scattered back from the flowing blood cells is partially collected by the same fiber and transmitted back to its entrance end. The reference beam is passed through a Bragg Cell to shift its frequency by f_1 (= 40MHz), so as to distinguish the forward blood flow from the reverse flow. Thus, the frequency of the reference beam is shifted to f_0–f_1. Optical heterodyne detection is obtained by mixing this reference beam with the light scattered back, resulting in a Doppler shifted frequency of $f_1 + \Delta f$. An avalanche photodiode, which provides a good signal to noise ratio, is employed as the photodetector. The photocurrent obtained from the avalanche photodiode is fed into a spectrum analyzer to analyze the Doppler shifted frequency of $f_1 + \Delta f$. The flow velocity is obtained from the frequency shift observed on the spectrum analyzer, while the flow direction is distinguished by the sign of the Doppler shift, i.e., if the signal appears on the right of the reference signal f_1 on the spectrum analyzer, it is forward flow and vice versa.

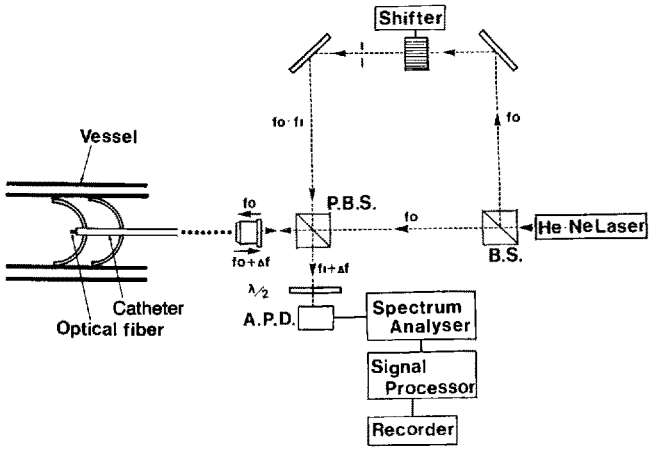

Fig. 1. Schematic diagram of a catheter-type laser Doppler velocimeter (LDV) using an optical fiber

Our previous experiments [21, 22] using this system showed that the sampling volume of this system is small, (approximately $\pi * 0.025^2 * 0.1\text{mm}^3$) and the temporal resolution is about 8 ms. A Doppler shift frequency (Δf) of 1MHz corresponds approximately to a blood velocity of 24 cm/s.

Configuration of the catheter tip

To keep the fiber tip in or near the axial region of the vessel, a spike-type catheter tip was designed (Fig. 2). The diameter of the optical fiber is 125 μm while that of the cover tube is 0.5 mm. Eight elastic silicon rubber spikes (diameter: 0.2–1.0mm) are arranged radially around the fiber tip with casting technique, and their tips were rounded out to prevent injury to the vascular wall. The catheter is guided into the vessel by an 8-F guide catheter (*right side* of Fig. 2). After the 8-F guide catheter is retracted, the spikes unfold and attach themselves to the vascular wall (*left side* of Fig. 2). This enables the fiber tip to position itself in or near the axial region of the vessel. In addition to monitoring of the blood flow velocity in or near the axial region, volume flow rate can also be estimated by measuring the vessel diameter angiographically.

Velocity measurement in model flow channel

To investigate the accuracy of flow measurements using our catheter-type laser Doppler velocimeter, we measured the flow velocity in a model flow channel (length: 2000 mm, inner diameter: 10 mm) made from Perspex glass (Fig. 3). The flow system consisted of a centrifugal pump, a distribution reservoir, a measuring section (straight and curved tubing), and a stopcock valve. The outlet of the centrifugal pump was connected to the distribution reservoir by rubber tubing, and the outlet of this reservoir was coupled to the flow channel. The test sections, i.e., the straight and curved tubing, were connected in series. The velocities in the straight tubing were measured at a point approximately 1000 mm from the inlet to the channel, and the distance from the inlet to the measuring point in the curved tubing was approximately 1600 mm.

Glycerine solution (1.3 centipoise) mixed with 2% v/v poster paint and 0.9% NaCl was used as the perfusate, because the light-scattering characteristics and viscosity of this mixture are very similar to those of the blood. Saline was used

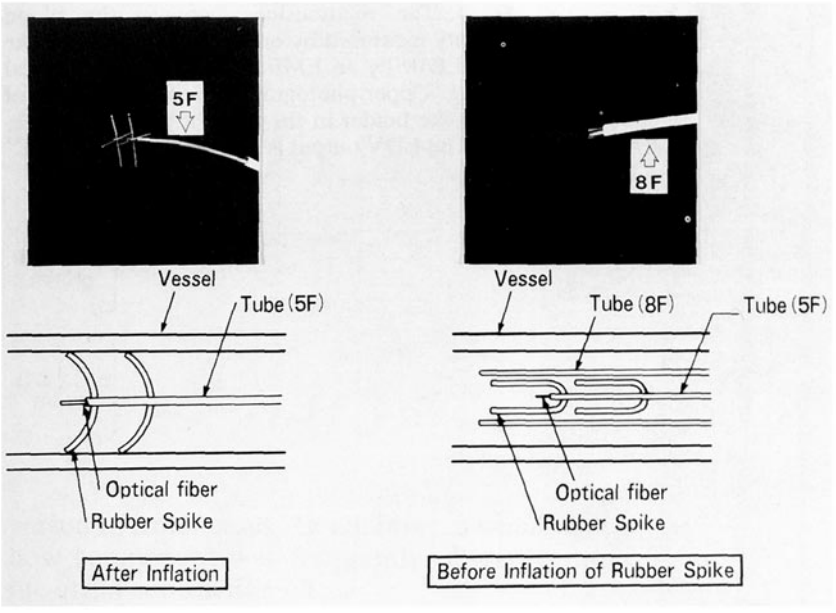

Fig. 2. Photographs and schematic drawings of the spike-type catheter tip. Configuration when the spikes unfold (*left*), and when the spikes fold into the catheter tube (*right*). Spike diameter is 0.2 mm

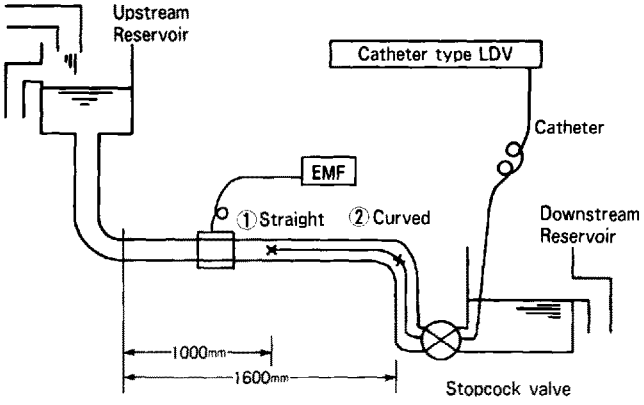

Fig. 3. Flow system to compare the flow velocity measured by our catheter LDV with that by an electromagnetic flowmeter (EMF). The test sections, i.e., straight and curved tubing, are connected in series. In this drawing, the fiber-catheter is inserted from the downstream reservoir to measure forward flow

as a conducting medium for the electromagnetic flowmeter (NIHON KOHDEN, MFV 1200). The perfusion pressure head was maintained at a constant level by the reservoir which was equipped to handle perfusate overflow. The flow rate was controlled by the stopcock valve at the end of the tubing. The dynamic flow was superimposed on a steady flow, using a stopcock valve adjustable to a step function to evaluate the step response of the velocimeter. The volume flow rate was measured by an electromagnetic flowmeter. The catheter was first inserted retrogradely into the flow channel from the outlet and placed at each test section (1 and 2 in Fig. 3).

Animal experiments

Five mongrel dogs weighing 12–29 kg were anesthetized with pentobarbital sodium, intubated, and ventilated by a constant volume respirator. The chest was opened by median sternotomy and left lateral thoracotomy, and the heart was suspended in a pericardial cradle. The proximal portion of the left anterior descending artery measuring approximately 5–7 mm was isolated. The cuff of the electromagnetic flowmeter was then placed around it. The laser Doppler catheter was inserted into the great cardiac vein via the coronary sinus, from the right jugular vein. After ensuring that a stable velocity waveform was being recorded, the fiber tip was fixed at that position by the silicon rubber spikes. The position of the catheter tip was monitored with the high frequency (25MHz) ultrasound echo imaging system (Omron, spatial resolution: 0.2 mm). The phasic blood flow velocity waveform was measured, and the reactive hyperemic response was evaluated after 20 s occlusion of the left anterior descending artery. Additional experiments were performed in two dogs to compare the velocity waveforms measured by the laser Doppler catheter with those measured by our 20 MHz 80 channel ultrasound Doppler velocimeter [23]. The great cardiac vein was isolated, and a cuff was placed around the vessel. The ultrasound Doppler probe was accessed to the great cardiac vein through a small hole in the cuff. The ultrasound Doppler velocity measurements were made at a sample point near the central axial region.

Results

Accuracy of the flow velocity measurement

Figure 4 shows the relationship between the laser Doppler velocimeter output voltage and the volume flow rate of the steady state flow in the straight model tubing. The volume flow rate was changed by altering the height of the reservoir, and was measured by an electromagnetic flowmeter. Velocity measurements were performed by extension of the fiber tip from the end of the catheter by 3mm. An excellent linear relationship was found between the output voltage and the volume flow rate (straight: $r = 0.982$; curved:

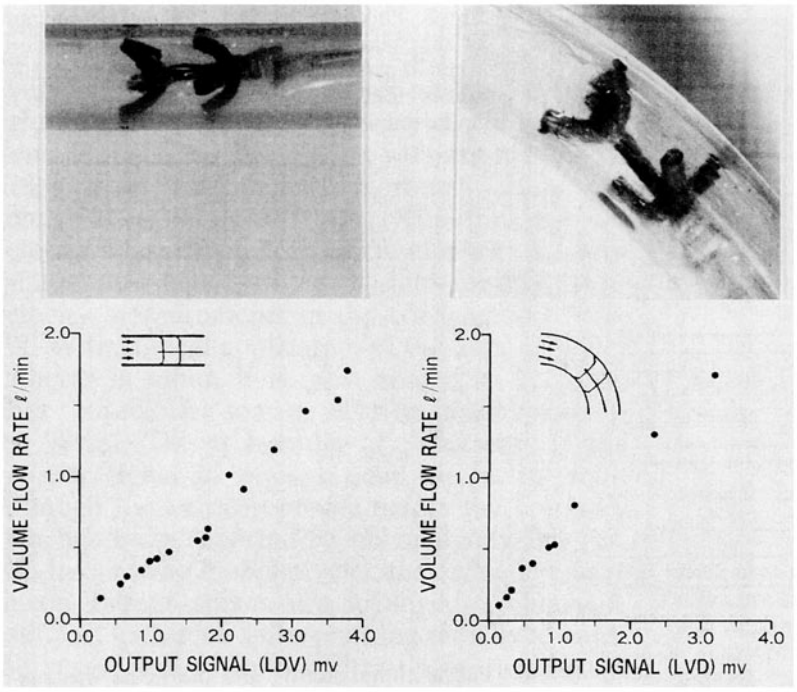

Fig. 4. The relationships between the blood velocity measured by our catheter LDV and the blood flow by an EMF, for straight and curved tubing. Upper photographs show the position of the spike holder in the straight and curved tubing. The LDV output is represented by voltage

r = 0.996), thus indicating that our velocimeter is accurate for measurements of flow velocity. The location of the catheter tip is shown in the *upper* panel of Fig. 4. It should be noted that the fiber tip was always placed near the central region of the tube by the spike holder. The position of the fiber tip in the curved tubing, however, deviated slightly from the axis. The regression line in the curved tubing was,

$$Y = 0.528x + 0.059$$

where Y is the laser Doppler velocimeter output, and X is the volume flow rate. The difference in the coefficient of X in the straight ($X = 0.445$) and the curved tubing was not statistically significant. The measurement of reverse flow may not be important for monitoring coronary vein flow, since the reverse flow component is usually small, or absent.

Figure 5 shows a comparison of the response of the laser Doppler velocimeter output to a stepwise increase in the perfusion pressure with that of an electromagnetic flowmeter. The velocity responses by the laser Doppler velocimeter and the electromagnetic flowmeter coincided well, indicating that our catheter system has enough temporal resolution to analyze pulsatile blood flow velocities. The correlation coefficients between the response by the laser Doppler velocimeter and that by the electromagnetic flowmeter were 0.998 and 0.997 for the straight tubing and curved tube, respectively.

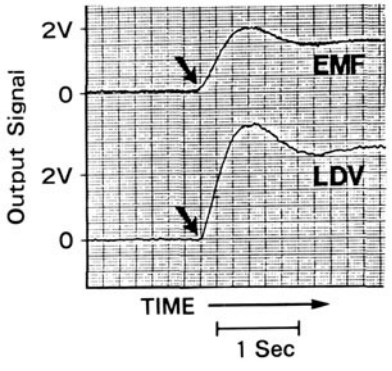

Fig. 5. Comparison of the transient blood velocity response by the catheter LDV with the flow recorded by an EMF. Note that the time courses of the velocity and flow responses coincide well with each other

Measurements of blood flow velocity in the great cardiac vein (GCV)

Figure 6 shows a typical trace of blood velocity in the great cardiac vein measured with this catheter system. Although the great cardiac vein flow velocity pattern was generally quite labile, this pattern represents one of the typical characteristics of the coronary vein flow, i.e., a systolic-predominant pattern. The great cardiac vein flow velocity increased around the beginning of the ventricular ejection and decreased gradually after the peak formation at the end of ejection. In addition to this main peak, a small forward flow component was found during the isovolumic contraction phase in this case. This isovolumic velocity component was changeable, i.e., it flattened or re-

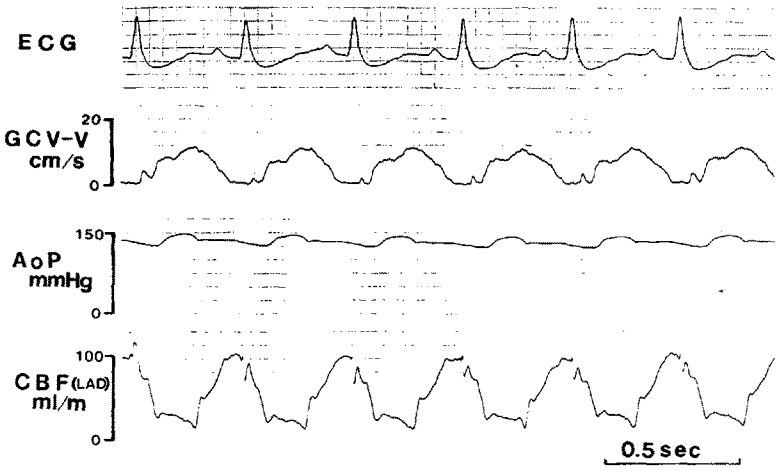

Fig. 6. A representative tracing of the velocity waveform in the great cardiac vein (GCV) measured by our catheter LDV. GCV-V GCV blood flow velocity, AoP aortic pressure, CBF blood flow in the left anterior descending artery (LAD) measured by an EMF

versed in some cases. In addition, a small reverse flow component was frequently observed during the atrial contraction phase.

Figure 7 shows the blood velocity waveform of reactive hyperemia after a 20 s occlusion of the left anterior descending artery. The velocity waveform under the control conditions in this case showed a two-peaked pattern. After reopening of the left anterior descending artery, the great cardiac vein velocity increased with a time lag on the order of 1–2 sec. As the velocity increased, the waveform initially showed a two-peaked pattern similar to that seen under the control conditions but gradually it exhibited a single, sharply peaked pattern when the velocity approached the maximum. As the velocity decreased from the maximum, the waveform again showed a two-peaked pattern. In addition to evaluation of the change in the phasic pattern during reactive hyperemia, the coronary flow reserve can also be evaluated by the response of the mean velocity during each cardiac cycle, after reopening of the left anterior descending artery. The small forward velocity components during the left anterior descending artery occlusion may be caused by collateral circulation and/or veno-venous anastomosis. This flow component did not change significantly throughout the period of occlusion. Figure 8 shows an example of the velocity waveform measured by the catheter type laser Doppler velocimeter, and by the 20 MHz 80 channel cuffed ultrasound velocimeter. It should be noted that the velocity waveform obtained with the laser Doppler catheter was in a good agreement with that measured by the external velocimeter, although small fluctuations were seen in the ultrasound Doppler tracing.

Figure 9 shows the high frequency ultrasound echo image of the great cardiac vein and the catheter tip in the vessel. We confirmed that the catheter tip was always fixed near the central axial region in the vessel by the spike holder.

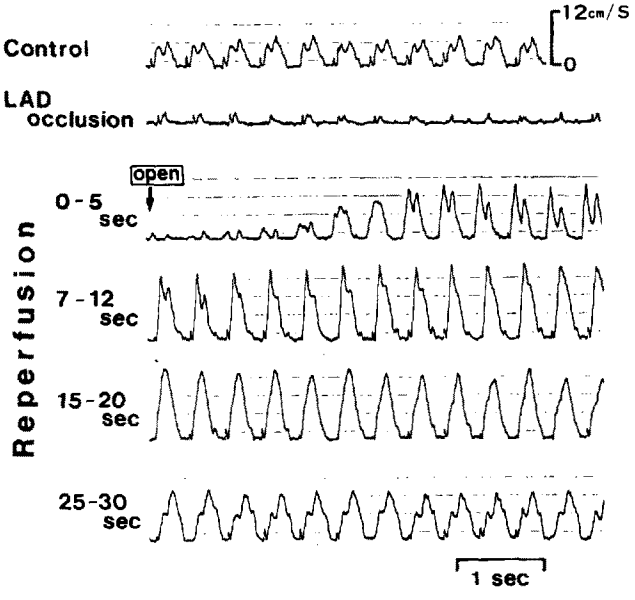

Fig. 7. A typical recording of the reactive hyperemic response in the great cardiac vein (GCV). Control: GCV blood flow velocity prior to LAD occlusion. LAD occlusion: the GCV blood flow velocity during LAD occlusion. Perfusion: GCV blood flow velocity response after reopening the LAD

Discussion

The major contribution of our study is the development of a laser Doppler velocimetry catheter for stable monitoring of phasic (and mean) coronary vein flow, including reverse flow. We utilized a laser Doppler velocimeter with an optical fiber previously developed in our own laboratory for the catheter system.

One of the most important techniques required when using a laser Doppler catheter is the placement of the fiber in a coronary vein, with the tip directed in or near the axial region in the vessel. For this purpose, we designed a special holder with eight elastic silicon rubber spikes. We confirmed that the fiber tip was kept in or near the

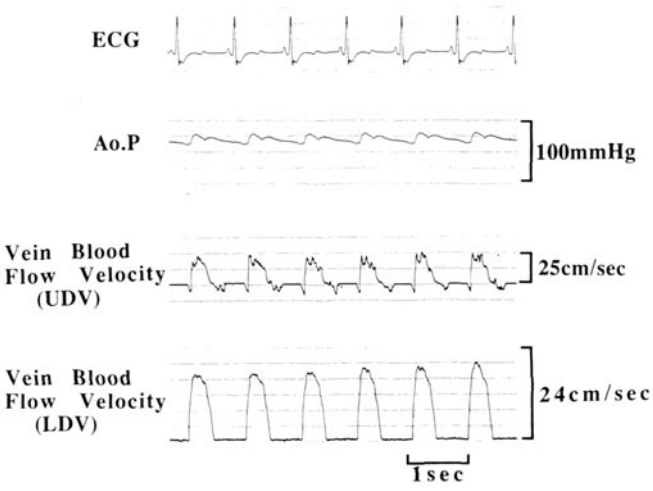

Fig. 8. Tracings of the blood velocity waveforms in the great cardiac vein of a mongrel dog measured by the catheter-type laser Doppler velocimeter (*bottom*), and a 20 MHz 80 channel cuffed ultrasound velocimeter (*second from the bottom*). *AoP* aortic pressure, *UDV* ultrasound Doppler method, *LDV* laser Doppler method

central axial region by this holder in the model tubing experiment (Fig. 4). Kilpatrick et al. inserted a fiber-optic probe with an external diameter of 0.3 mm through a polyethylene tube into the coronary sinus [19]. They tried to keep the fiber tip away from the wall by attaching a polyethylene tube to the center of the coronary sinus cannula. However, our catheter is less restrictive to flow, since we remove the catheter tube from the coronary sinus during measurement. Moreover, the spike holder exhibits an excellent ability to sustain the fiber tip in or near the axial region in the vessel. This was confirmed by the high frequency ultrasound echo image (Fig. 9). The shape of the coronary vein may vary during the cardiac cycle, because of its high compliance. However, the echo imaging indicated that the variation was minimized by the rubber spike system. In clinical application, the coronary sinus and great cardiac vein dimensions may vary from person to person, and may be influenced by coronary vein pressure. Accordingly, rubber spikes with various sizes will be necessary to cover the variation in vessel dimensions.

The linear correlations between the flow velocity and the volume flow rate in both straight and curved model tubing indicate the accuracy of our blood velocity measurements. We also observed that the velocity waveform obtained with the laser Doppler catheter was in a good agreement with that measured with the external 20MHz ultrasound velocimeter. Furthermore, one of the important characteristics of the laser Doppler catheter is its high accuracy in the measurement of flow velocities. However, for the same volume flow rate, the velocity measured in the straight tubing was slightly higher than that in the curved tubing, although the difference was not statistically significant and not practically important. The lower velocity in the curved tubing may be due to the angle developed between the fiber and the stream line, and to skewing of the velocity profile across the tubing. The temporal resolution of our systems is approximately 50Hz with sampling performed every 8 ms.

The most important feature of our laser Doppler catheter is its ability to continuously measure the phasic coronary vein flow, which may provide information about myocardial blood perfusion and the effect of cardiac contraction and relaxation on intramyocardial blood compartment.

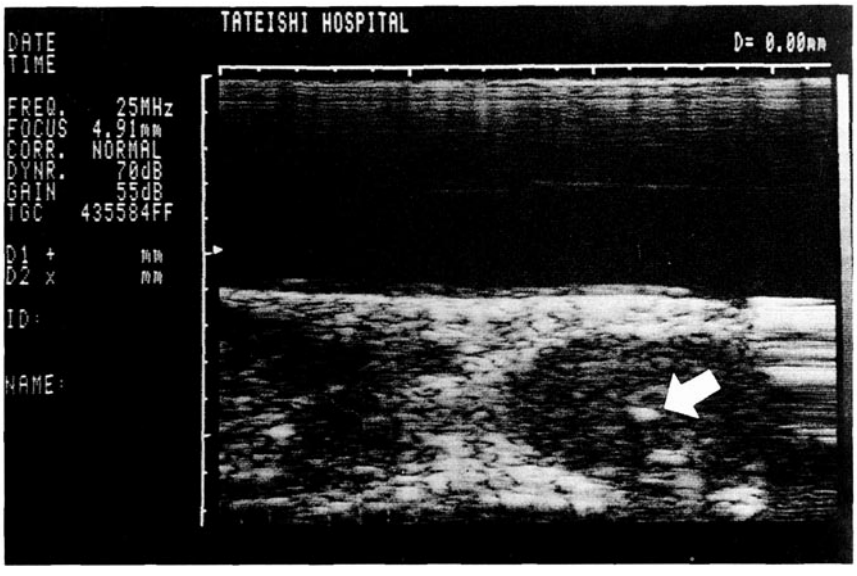

Fig. 9. An ultrasound echo image of the great cardiac vein. The catheter tip is held by the four rubber spikes in or near the axial region of the vein (*white arrow*)

Anrep et al. and Wigers have studied the phasic pattern of drained coronary sinus flow using a hot wire method, and a pressure difference velocimeter, respectively [24]. In the 1960s, Scholtholt and Lochner [25] and Stein et al. [26] measured the coronary sinus blood flow with a catheter-tipped electromagnetic flowmeter. There is general agreement that the flow dynamics in the coronary vein is characterized by the phasic flow predominant in systole, although opinions regarding minor flow components remain controversial. In our previous study, we measured the great cardiac vein blood flow velocity in dogs using a laser Doppler velocimeter with an optical fiber [20]. The fiber was inserted into the vessel from the side wall of the great cardiac vein with the aid of a cuff. We observed the following: (1) The great cardiac vein blood flow velocity increased around the onset of left ventricular ejection, and then decreased gradually toward the zero flow velocity line after the peak formation at mid- or late- systole. (2) In addition to the main systolic flow wave, one or two small wave components were frequently observed during the atrial contraction phase and/or the isovolumic contraction phase. (3) Pharmacological intervention, e.g., isoproterenol, accelerated the rate of the rise in the systolic flow. These findings indicate that measurement of the phasic waveform of the coronary vein flow velocity can provide useful information for the clinical evaluation of coronary hemodynamics.

Although the regional patterns of coronary vein drainage are variable and complex, Robert et al. indicated that the blood flow of the great cardiac vein is remarkably free of left circumflex inflow [27]. We also observed a close correlation between left anterior descending artery flow and great cardiac vein flow during long diastole [17] (Fig. 6). Accordingly, we measured the blood flow velocity during reactive hyperemia in the great cardiac vein, which is linked closely to the left anterior descending artery. Following left anterior descending artery occlusion, the great cardiac vein velocity decreased significantly. Following reopening of the left anterior descending artery, the great cardiac vein flow velocity increased, showing a reactive hyperemic response, and then returned to the control level. The coronary flow reserve can be evaluated from the magnitude of the augmentation of the great cardiac vein flow velocity. However, variable residual flow velocities were measured during left anterior descending artery occlusion. These residual velocities may be due to blood draining from vascular beds other than the left anterior descending artery, i.e., collateral circulation and/or veno-venous anastomoses. Recently Cohen et al. [28] examined the hemodynamic interdependence of the left anterior descending coronary artery and the great cardiac vein. Although they did not differ under baseline conditions, left anterior descending artery occlusion caused only a 56% decrease in great cardiac vein flow, whereas the degree of peak great cardiac vein flow during reactive hyperemia was less than that of peak left anterior artery flow by 40%. Thus, this underestimation should be considered when the reactive hyperemic response is evaluated from great cardiac vein flow. Pharmaceutical vasodilation, e.g., papaverine administration, may provide more accurate data for the evaluation of coronary flow reserve by vein outflow.

Although the aim of this study was to employ our laser Doppler catheter in making blood velocity measurements in the coronary vein, it may also be applied to the monitoring of the blood flow in the coronary artery. In the former case, the catheter transducer should be directed upstream (towards the flow), while in the latter case it should be directed downstream. The direction of the probe is important, since the flow perturbation varies with the orientation of the probe. In the case of coronary artery velocity measurements, the direction of the flow is usually away from the catheter, and the flow field may be easily disturbed [29]. Recently, we found that a dual fiber laser Doppler velocimeter is effective for the accurate detection of flow away from the catheter [30, 31]. In this system, two fibers (one for light emission, and the other for light collection) are placed side by side so that the sensing field can be extended away from the fiber tip. This dual fiber laser Doppler velocimeter may be useful for the measurement of coronary artery flow velocity.

In clinical situations the catheter may be left in place for a significant period of time. However, antithrombogenicity may be a major problem to be solved, and a slow release of physiologically active substances, such as heparin, from the surface of catheter could be effective. Biocompatible elastomers in which anticoagulant/compliment inhibitor is dispersed may also ensure antithrombogenic-

In conclusion, we developed a laser Doppler catheter which was useful for monitoring both phasic and mean coronary vein blood flow velocities. Both the model and animal experiments demonstrated that our system held promise for accurate measurements of pulsatile blood flow velocities in the vessel. We are presently attempting to miniaturize the catheter so that transition from animal experiments to clinical application will be possible.

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