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● *Original Contribution*

A NOVEL *IN VIVO* PROCEDURE FOR VOLUMETRIC FLOW MEASUREMENTS

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Abstract—We report on a novel procedure for invasive volumetric blood flow measurements using a commercially available Doppler flow wire system, which could, until now, only measure flow velocity. We here describe a method applicable *in vivo* to generate both velocity and cross-sectional area information from the same pulsed-wave Doppler signal for volumetric flow assessment. We demonstrate its feasibility and validation *in vivo* in pig coronary arteries. Our Doppler-derived volumetric flow measurements were compared with the respective transit-time flow and showed an excellent correlation ($r = 0.969$; $p < 0.0001$). Agreement between transit-time and Doppler-derived flow measurements could be observed for flow conditions ranging from 30 to 180 mL/min. The mean values for the two methods were 71.4 ± 43.7 mL/min and 71.3 ± 42.2 mL/min, respectively. We conclude that this technique might possibly be introduced into future clinical practice as an invasive procedure of choice for the assessment of volumetric blood flow. (E-mail: karjer@usz.unizh.ch)

Key Words: **Volumetric flow, Doppler flow wire, Doppler signal power.**

INTRODUCTION

As given in eqn (1), volume flow (Q) in any vessel is defined as the product of mean flow velocity (V_{mean}) and cross-sectional area (A):

$$Q = V_{mean} A. \quad (1)$$

There is to date no commercially available system that allows measurement of both velocity and cross-sectional area with a single catheter. Determination of cross-sectional area requires the additional use of either angiography or intravascular ultrasound (US), which may be time-consuming and, often, too demanding for clinical use. Therefore, in daily clinical routine, volumetric blood flow measurement relies on blood flow velocity alone (Doucette et al. 1992), assuming that the vessel diameter and the velocity profile remain constant during different flow conditions (Vanyi et al. 1993; Deychak et al. 1995). This assumption, however, is wrong at high flow conditions when flow-dependent vasodilation may occur, inducing changes in flow velocity profile. Another fundamental limitation of the actual clinical routine procedure is the fact that the currently used Doppler flow wire systems allow assessment of average peak velocity (*APV*), but not of V_{mean}. Subsequently, for the calculation of V_{mean} from *APV*, a constant coefficient of 0.5 is commonly used ($V_{mean} = 0.5\ APV$). Unfortunately, this does not hold true for pulsatile flow (Nichols and O'Rourke 1990).

A prerequisite for accurate volumetric flow measurement is that the measurement itself is independent 1. from velocity profile, 2. from vessel area, and 3. from the angle between the vessel axis and the US beam. A transcutaneous method for flow measurement, which fulfills all these three prerequisites has been described by Hottinger and Meindl (1979) more than 2 decades ago. They used a dual beam pulsed-wave Doppler system, of which one beam is a wide beam capable to insonate the total cross-sectional area of the vessel, whereas the second beam is a narrow beam with a known cross-sectional area within the vessel. V_{mean} is measured with the wide

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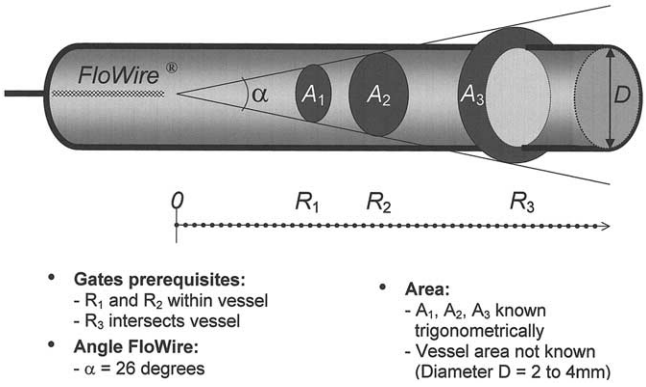

Fig. 1. Flowire system. Measurements at gate depths 1 and 2 are used to correct the received power of gate 3 for attenuation and scattering. The (corrected) power received from gate 3 corresponds to the cross-sectional area of the vessel and, at this position, V_{mean} is calculated as $V_{mean} = M_1/M_0$.

beam (insonating the entire cross-sectional area) and the vessel cross-sectional area is measured by utilizing the power returns of both beams, as follows. The cross-sectional area of the vessel is determined by the ratio of Doppler power returns of the two beams using the known area of the narrow beam. The Doppler power returns of the beam represent the sum of all intensities of each Doppler shift frequency, which is proportional to the total number of all moving erythrocytes within the cross-sectional area.

We have recently validated, in an *in vitro* study, a newly developed method for the calculation of volumetric flow (Jenni et al. 2000). We now show, for the first time, the *in vivo* feasibility of our novel technique for direct volumetric blood flow measurement by simultaneous assessment of vessel cross-sectional area and V_{mean} solely from received Doppler power. Our method is based on the Hottinger and Meindl principle; however, using a commercially available single-beam Doppler flow wire system into which our specific software for calculation of the zeroth (M_0) and the first (M_1) Doppler moments was implemented by the manufacturer following our suggestions (Jenni et al. 2000).

METHODS

Doppler flow wire

The Doppler wide-beam flow wire (FloWire, from Cardiometrics, Mountain View, CA), is a torquable, guidable wire with a nominal diameter of 0.35 mm and a length of 175 cm. It is capable of entering small and distal branches of the coronary tree. At the tip of the guidewire, a 12-MHz piezoelectric crystal is mounted. The forward-directed US beam diverges ± 13° from its axis as measured (by the manufacturer) at the −6-dB points of the ultrasonic beam pattern (two-way beam width). The Doppler guidewire is coupled to a commercially available Doppler system (FloMap®, Cardiometrics). The sample volume depth can be moved along the beam axis at discrete steps of 0.13 mm. Doppler signals were sequentially taken with a single-gate pulsed Doppler. It takes one *R–R* interval to take one sample at one depth.

Determination of volumetric flow

According to the Parceval's theorem (Challis and Kitney 1991), the received Doppler power, which equals M_0 of the Doppler spectrum, is proportional to the insonated area at the respective gate depth. In addition, the Doppler power received by the transducer depends on the attenuation function of the medium, the scattering function and the sample volume size (Challis and Kitney 1991).

Three Doppler power measurements are necessary (Fig. 1): M_0 measurements at gate depths R_1 and R_2 are used to correct the received power of gate R_3 for attenuation and scattering. Thus, the (corrected) power received from gate R_3 corresponds to the cross-sectional area of the vessel and, at this position, V_{mean} is calculated as $V_{mean} = M_1/M_0$. Finally, V_{mean} and cross-sectional area were calculated according to eqn (2), as described previously (Jenni et al. 2000).

$$Q = \overbrace{k\frac{M_{1,3}}{M_{0,3}}}^{V_{mean}} \times \overbrace{\frac{A_2^{N+1}}{A_1^N} \times \frac{M_{0,1}^N M_{0,3}}{M_{0,2}^{N+1}} \times \left[1 - \frac{r}{R_2}\right]^{4N} \times \left[1 + \frac{N_r}{R_2}\right]^4}^{\text{area}(A)}, \quad (2)$$

where Q = volumetric flow; $k = c/(2f_s)$; c = speed of sound in the medium; f_s = emitted frequency; $M_{0,n}$ and $M_{1,n}$ = zeroth and first Doppler moments of sample volume n at gate distance R_n; r = $R_2 - R_1$; $N = (R_3 -$

$R_2)/(R_2 - R_1) = (R_3 - R_2)/r$, and A_1, A_2, A_3 represent the area A at the respective gate depths R_1, R_2, R_3.

The volumetric flow value Q (*i.e.*, the product of $V_{mean} \times$ area (A) is independent of the angle between the beam and the bloodstream, although each term alone is not independent. This is due to the fact that the cosine of the angle is once in the numerator and once in the denominator and, thus, cancels out. In addition, the term in eqn (3):

$$\left[1 - \frac{r}{R_2}\right]^{4N} \times \left[1 + \frac{r}{R_2}\right]^{4} \quad (3)$$

equals 1 for equidistant gate depths. Otherwise, the term compensates for nonequidistant gate depths.

Doppler moment measurements

Doppler moments were measured at several consecutive gate depths, increasing by 0.39-mm steps for a beam diameter of between 1 and 5 mm. This ensures to include, on the one hand, gate positions small enough for the Doppler beam to lie completely within the vessel lumen ($R1$, $R2$) and, on the other hand, gate positions large enough (R_3) for the beam to intersect a vessel of unknown diameter between 2 and 4 mm (a representative range of coronary artery diameters). Special care was taken for optimal positioning of the Doppler flow wire to obtain high-quality Doppler spectra, which are characterized by strong signals in the high-velocity range and by a sharply defined envelope.

All moments M_0 and M_1 calculated at the different gate depths were stored on a laptop PC for further analysis. During the offline processing, only data from those gate position combinations complying strictly with the mathematical condition in eqn (4) were used for the calculation of volumetric flow:

$$\frac{M_{0,1}^{N}\, M_{0,3}}{M_{0,2}^{N+1}} = 1 \quad (4)$$

If eqn (4) is fulfilled, the term area (A) in eqn (2) equals vessel area.

Experimental procedure

The study was approved by the ethical committees of both the canton of Zurich (Kantonale Kommission für Tierversuche) and the University Hospital of Zurich, Switzerland.

Measurements were performed in the left anterior descending (LAD) coronary artery of three pigs using a Doppler wide-beam flow wire. One pig was used for validation of the correlation between time-collected and transit-time flow. Blood flow provided by a roller pump to the mammary artery bypass graft was assessed by a transit-time flow probe placed around the inlet tubing. Transit-time blood flow was calibrated against the time-collection method, while the free flow collected during a period of 15 s was measured.

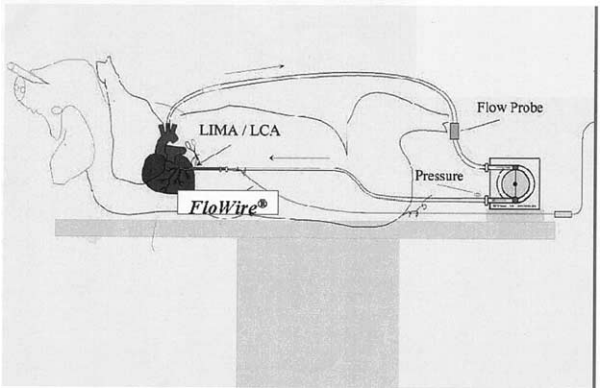

Fig. 2. Experimental procedure. See Methods section for detailed explanation.

Surgery was performed under general anesthesia. After medial sternotomy, the left internal thoracic artery (LITA) was prepared for anastomosis on the LAD coronary artery. Side branches were clipped over the whole length of the LITA graft as well as the first septal branches of the LAD over a length of 3 cm to achieve a flow without perfusion of the septal branches distal to the anastomosis. A vessel loop was then applied around the origin of the LAD to avoid blood inflow through the native LAD. These manipulations ensured that the flow at the site where it was measured exactly corresponds to the flow within the LITA/LAD anastomosis further downstream. Throughout the procedure, animals were under heparin.

The aortic root cannula was connected to a pediatric roller pump (Stöckert; Munich, Germany). The distal end of the system was connected to a bifurcated port system, allowing perfusion of the LITA to LAD graft and to introduce the flow wire. The correct position of the flow wire (one cm distal of the LITA to LAD anastomosis) was controlled visually. Finally, the proximal vessel loop was snared, so that only pump flow could perfuse the LAD. During the measurements, pump flow was maintained between 30 and 180 mL/min.

Before the extracorporeal system was run, pump flow was adjusted by altering the occlusion of the roller pump. Accuracy of flow was additionally controlled by a transit-time flow probe placed around the outlet tube, as the pump was running in a closed circuit preoperatively. The experimental procedure is depicted in Fig. 2.

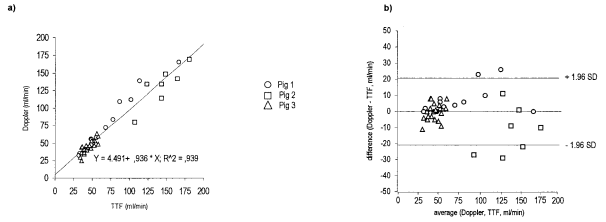

Fig. 3. Regression analysis. (a) Correlation between Doppler-derived volumetric flow and time-collected flow. (b) The average blood flow values of the two measurements are plotted against their difference according to Bland and Altman (1986). Note that more than 95% of all measurements ($n = 39$) are within ± 1.96 SD.

RESULTS

There was a high correlation between time-collected and transit-time flow: $R^2 = 0.99$; $p < 0.001$. Flow ranged from 5 to 170 mL/min (data not shown). The overall mean values ± 1 SD of the transit-time and Doppler-derived volumetric flows were 71.4 ± 43.7 mL/min and 71.3 ± 42.2 mL/min, respectively.

A high correlation was found between transit-time and Doppler-derived flow values (r = 0.969; $p < 0.0001$, Fig. 3). The regression line lies close to the line of equality, indicating an excellent agreement for transit-time and Doppler-derived flow measurements over a wide range of flow conditions (from 30 to 180 mL/min). This is confirmed by plotting the mean difference against the average values according to the test proposed by Bland and Altman (1986) proving that there was no bias and that the SD (10.7 mL/min) of the mean difference was small (Fig. 3).

DISCUSSION

The procedure we describe represents the first method for invasive *in vivo* volumetric flow measurements using a commercially available Doppler flow wire system. Although this procedure with the commercially available Doppler system may be applied for volumetric blood flow measurement in any artery with a diameter less than 4 mm, it might be of particular interest for the assessment of coronary blood flow and coronary flow reserve (CFR; ratio of hyperemic over resting flow). For the assessment of CFR, hyperemic flow is induced by vasodilator agents such as adenosine, which affects both coronary vessel diameter and flow profile. Therefore, the actual and widely used assessment of CFR by using *APV* alone is flawed by fundamental limitations and must be judged with caution, as it may produce misleading results (Kaufmann and Jenni 2000). This current practice is potentially hazardous because the results often directly influence clinical decisions with regard to revascularization therapy (Bach et al. 1995). Our novel system overcomes these limitations. It accounts both for changes in flow velocity profile and for changes in vessel cross-sectional area because the whole term Q of eqn (2) is independent from the angle between vessel and beam. It can, therefore, provide accurate measurements of coronary blood flow and CFR and may become of great value in routine clinical practice. In addition, by decreasing the transducer frequency (and, thus, increasing the beam angle) our technique can be applied to vessels of any size, including the aorta. In the near future, a multigate system simultaneously acquiring the Doppler moments at consecutive gate depths will considerably speed up the measurements and facilitate rapid introduction of the procedure into clinical use.

For our technique, we have assumed that the transducer generates uniform acoustic intensity across the sample volumes because, theoretically, any non-uniformity of the intensity may affect the Doppler power spectrum. For homogenous scattering, exclusion of turbulent flow is another important prerequisite because the scattering power is a function of the variance in the packing or concentration of the cells within an acoustic volume, and this variance may increase in turbulent flow (Mo et al. 1990). Thus, for the reliable use of our technique, due care has to be taken to perform measurements in nonstenotic segments of coronary arteries (such as found proximal or distal of stenotic lesions in the presence of obstructive coronary artery disease) to avoid turbulent flow. A potential limitation of our technique is that only high-quality Doppler spectra tracings—necessitating optimal positioning of the flow wire—provide optimal results. However, this limitation applies even more to the conventional flow wire measurements. It is assumed that, if a high-quality Doppler spectrum is achieved, the catheter is centered. A further limitation consists in the fact that large vessels (> 0.4 cm) cannot be entirely insonated. Because registration and selection of high-quality tracings may depend on the operator's experience, successful measurement with our technique may be subject to a learning curve. This, however, does not affect accuracy of the method because measurements with suboptimal positioning of the flow wire will be rejected; such measurements provide results that do not fulfill the mathematical condition of eqn (4).

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