Validation of a Doppler Guide Wire for Intravascular Measurement of Coronary Artery Flow Velocity

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Background. An improved intravascular ultrasonic Doppler device could aid the clinical assessment of coronary hemodynamics. We evaluated a new device consisting of a 12-MHz piezoelectric transducer integrated onto the tip of a 0.018-in. flexible, steerable angioplasty guide wire.

Methods and Results. Doppler spectra were recorded in model tubes with pulsatile blood flow and in-line electromagnetic flowmeter. In four straight tubes (i.d., 0.79–4.76 mm), the time average of spectral peak velocity (APV) was linearly related to blood flow (QEMF) \( (r^2=0.98 \text{ for each tube}) \). A Doppler-derived quantitative flow estimate (QD) was calculated as the product of vessel cross-sectional area and mean velocity, with mean velocity estimated as 0.5 \times \text{APV}. The slope of QD versus QEMF for the four tubes was near unity. APV was less accurate in a 7.94-mm straight tube and in tortuous segments. In four dogs, the left circumflex coronary artery (LCx) was perused from the femoral artery via a cannula with in-line electromagnetic flowmeter. Good-quality signals were obtained in proximal and distal LCx vessels 3.3–1.2 mm in diameter. APV varied linearly with QEMF \( (r^2 \geq 0.99 \text{ in the cannula}, r^2=0.93–0.99 \text{ in proximal LCx}, \text{ and } r^2=0.86–0.99 \text{ in distal LCx}) \). QD was calculated by quantitative angiography to determine proximal LCx diameter. For all dogs combined, the slope of QD versus QEMF was 0.95 in the cannula and 0.85 in the proximal LCx.

Conclusions. The Doppler guide wire measures phasic flow velocity patterns and linearly tracks changes in flow rate in small, straight coronary arteries. It should facilitate measurement of phasic coronary flow velocity during coronary angiography and angioplasty. (Circulation 1992;85:1899–1911)

KEY WORDS • coronary circulation • ultrasound • echocardiography, Doppler • catheters

Coronary flow velocity measurement by ultrasonic Doppler systems in laboratory and clinical research settings has provided information crucial to modern theories of coronary hemodynamics. Methodological limitations, however, have hampered the development and widespread use of ultrasonic Doppler in coronary hemodynamic evaluation for clinical purposes. An improved intravascular Doppler system could increase the ease and usefulness of coronary hemodynamic measurements during routine cardiac catheterization and percutaneous transluminal coronary angioplasty (PTCA).

Coronary flow velocity measurement has several potential clinical applications. Extravascular Doppler probes placed directly onto the surface of a coronary artery have recorded phasic flow patterns in small distal branches of the epicardial arteries and in septal arteries and allowed analysis of their response to alterations in pressure and inotropy. They have also allowed description of characteristic changes in phasic flow velocity patterns distal to coronary stenoses during bypass graft procedures and have documented the effects of hypertrophy on coronary flow reserve. The use of direct extravascular probes is limited to open-chest procedures or animal experimentation, however. Coronary flow velocity has been measured in closed-chest humans by the transeosophageal route, but these measurements have been limited to the very proximal coronary arteries. Intravascular, catheter-based Doppler ultrasound devices have been used to measure coronary flow reserve and to calculate minimal stenosis area. The combination of subselective interrogation of the coronary arterial tree and applicability in closed-chest humans during catheterization and PTCA makes the intravascular approach attractive for many clinical applications.

Many improvements have been made since Benchimol and later Hartley and Cole introduced catheter-based Doppler systems in the 1970s. Currently used devices are composed of piezoelectric crystals mounted at the tip or on the side of catheters as small as 3F (1-mm o.d.). Most have a central lumen that can accommodate a standard 0.014-in. angioplasty guide.
wire to aid in subselective placement within the coronary tree. A device has been investigated\(^{13}\) that uses a 1-mm ring-shaped transducer affixed to the tip of an angioplasty balloon catheter.

Even at 1 mm in diameter, these devices significantly affect blood flow. A catheter with side-mounted transducer necessarily disturbs the flow velocity profile across the vessel in the sample volume because of the catheter shaft within the vessel at the point of interrogation. The shaft of a 1-mm-diameter catheter upstream from a forward-directed ultrasound beam also alters the flow velocity profile across the vessel, depressing the peak velocity of blood flow in the sample volume.\(^{14}\) In small distal vessels, significant obstruction of the vessel by the catheter may occur, altering baseline flow rate and inducing reactive hyperemia due to ischemia.

Another factor that has slowed the widespread application of this potentially valuable technology is the time and complexity that it has typically added to clinical procedures. Use of Doppler catheters during PTCA requires additional catheter exchanges, prolonging and disrupting the procedure.

A PTCA guide wire possesses many characteristics of an ideal delivery system for an intravascular Doppler ultrasound transducer. A 0.018-in.-diameter guide wire has a cross-sectional area of 0.164 mm\(^2\), only 21% of the cross-sectional area of a 1-mm catheter. It should create less disturbance of the flow profile downstream from its tip when placed within a vessel and can be passed into smaller arteries without causing significant stenosis. Its flexibility and steerability are specifically designed for crossing stenoses in coronary arteries and for stable, prolonged placement in the distal portion of an artery during angioplasty procedures. Guide wires have been used routinely and safely in diseased human arteries for years. If a Doppler-equipped guide wire is substituted for the standard guide wire, phasic coronary blood flow velocity measurements might easily be incorporated into PTCA without greatly complicating the procedure. Therefore, we evaluated a newly developed intravascular ultrasonic Doppler guide wire in both in vitro and in vivo models of the coronary circulation.

**Methods**

**Doppler Guide Wire**

The Doppler guide wire (Cardiometrics, Inc., Mountain View, Calif.) is constructed of a 175-cm-long, 0.018-in.-diameter, flexible and steerable guide wire with a 12-MHz piezoelectric ultrasound transducer integrated onto its tip (Figure 1). The forward-directed ultrasound beam diverges \(\pm 10^\circ\) from its axis as measured to the \(-6\) dB (round-trip) points of the ultrasonic beam pattern. This broad beam provides insonation of a relatively large area in the vessel of interest, sampling a large portion of the flow profile. In all our experiments, we used a pulse repetition frequency of 40 kHz, a pulse duration of 0.83 µsec, and a sampling delay of 6.5 µsec. The choice of these parameters determined that the sample volume was 0.65 mm thick by 1.7 mm in diameter and was located 5 mm beyond the guide wire tip.

The system coupled to the guide wire consisted of a Doppler instrument, a real-time spectrum analyzer, a videocassette recorder, and a video page printer. The Doppler instrument generated 12-MHz transmit signals to excite the piezoelectric transducer and processed the returning echoes to produce quadrature Doppler audio signals. The quadrature Doppler audio signals were processed by a real-time spectrum analyzer that uses on-line fast Fourier transform to provide a scrolling gray-scale spectral display. The frequency response of the system is determined by the spectrum analyzer, which calculates approximately 90 spectra per second. The spectral display and Doppler audio signals were recorded on videocassette for later review, and prints of the spectral display were provided by the video page printer. The Doppler system has since been upgraded to include simultaneous ECG recording and a software package to provide on-line computation of a variety of specified parameters, including instantaneous spectral
peak velocity and the time average of spectral peak velocity. Detailed specifications of the system are included in the “Appendix.”

We conducted in vitro experiments in plastic tubes of various sizes to evaluate the ability of the Doppler guide wire to measure pulsatile flow velocity in straight and tortuous tubes at different flow rates and to evaluate the effects of changing degrees of pulsatility on the velocity measurements. In vivo studies in dogs were conducted to evaluate the maneuverability and stability of the device within the coronary arterial tree, to assess the quality of phasic flow velocity spectra, and to evaluate the ability of the device to track changes in flow rate linearly in different portions of the coronary arteries in a beating heart. We also tested a method for quantifying volume flow rates based on blood velocity derived from Doppler measurements and vessel cross-sectional area obtained by direct measurement of model tubes or quantitative angiography of canine vessels.

**In Vitro Experiments**

Heparinized bovine blood was directed from a reservoir via a length of flexible tubing through a pulsatile roller pump (Masterflex, model 7520-25, Cole-Parmer Instrument Co.) and into one of five straight plastic tubes of known diameter (0.79, 1.59, 3.17, 4.76, and 7.94 mm). An in-line electromagnetic flow probe (model 300A, EMPICO) connected to a flowmeter (model FM 501D, Carolina Medical Electronics) (EMF) was used to measure the blood flow rate ($Q_{EMF}$). The EMF was calibrated by timed collection of blood into a graduated cylinder. A short segment of tubing was incorporated into the circuit by two Y- adaptors that bypassed the EMF, allowing frequent zero determinations during the experiment via occlusion of the EMF limb. The Doppler guide wire was introduced into the plastic tube of known diameter via a side port and advanced 20–60 cm (>20 times the tube diameter), where a fully developed parabolic flow profile would be expected at physiological flow rates and Reynolds numbers. The flow rate was varied while simultaneous EMF and Doppler measurements were obtained.

To test the effects of changing pulsatility on measured velocity, we held mean $Q_{EMF}$ constant while changing the pulsatility of flow over a wide range and recorded Doppler spectra at each level of pulsatility. Flow was established from the roller pump through the straight 3.17-mm tube, then the intrinsic pulsatility from the pump was damped by attaching a balloon to a side port in the circuit to act as a capacitor. This produced a nearly constant flow rate. The pulsatility of flow was then increased by rhythmic compression of the balloon while $Q_{EMF}$ was kept constant. By increasing the strength of compression in stepwise fashion, seven different degrees of pulsatility were produced. Doppler spectra were recorded at each level of pulsatility. This experiment was repeated at three different mean flow rates.

The effects of vessel tortuosity on flow velocity measurement were assessed in a model tube system with a 3.17-mm-diameter lumen forming three semicircular curves with radii of 1, ½, and ¼ in. with in-line EMF and roller pump. The 3.17-mm-diameter tubular channel was bored into a solid plastic block to ensure a uniform circular lumen at all points along the system.

The wire was first guided through the entire model in the direction of blood flow, then Doppler spectra were recorded at seven different positions as the wire was pulled back through the model while $Q_{EMF}$ was held constant. At each measuring point, the wire was rotated until the signal was optimized. This “pullback” procedure was performed four times with two different constant mean flow rates in both directions. The wire was always introduced in the same direction as the flow of blood, so that the sample volume remained downstream from the transducer. After the pullback maneuvers, the wire was reinserted to position the sample volume in the tightest curve of the model, with a radius of ¼ in. Nine Doppler spectral measurements were made at different values of $Q_{EMF}$ to determine the linearity of the relation between Doppler measurements and $Q_{EMF}$ in this tortuous segment.

**In Vivo Experiments**

The protocol was approved by the Committee on Animal Research at the University of California San Francisco. All animals were treated in accordance with the principles of the American Physiological Society. Four mongrel dogs (weight, 20–36 kg) were premedicated with fentanyl and droperidol (Innovar-Vet, Pitman-Moore), and anesthesia was induced with sodium pentobarbital (25 mg/kg i.v.). The dogs were intubated with a cuffed endotracheal tube and ventilated with room air supplemented with oxygen (2–6 l/min) in room air by a Harvard respirator. Arterial blood gases were measured frequently and maintained in the normal range by adjustment of the ventilator settings. Additional sodium pentobarbital was administered as necessary throughout the experiment to maintain adequate anesthesia. A fluid-filled catheter was introduced through the right femoral artery for continuous aortic pressure monitoring. A left thoracotomy was performed in the fourth or fifth intercostal space, and the heart was exposed and suspended in a pericardial cradle. Epicardial pacing electrodes were sewn onto the left atrium and connected to a stimulator. The proximal left circumflex coronary artery (LCx) was dissected free of the surrounding tissue. Heparin was given (10,000 units i.v. as an initial bolus and 2,000 units/hr). A shunt circuit was established from the left femoral artery to the LCx so that the flow rate in the LCx could be directly controlled and quantified (Figure 2). The circuit consisted of a large-bore catheter placed in the left femoral artery and connected by a length of plastic tubing to a stainless steel cannula (i.d., 2.9 mm; o.d., 3.5 mm). The same EMF used in the in vitro experiments was recalibrated and placed just proximal to the cannula for measurement of blood flow through the circuit. A short bypass limb in the circuit allowed frequent EMF zero determinations by clamping the flowmeter limb without cessation of coronary flow. The cannula was introduced via a left subclavian arteriotomy through the ascending aorta and left main coronary artery into the proximal LCx, where it was fixed in place with a ligature. The cannula was equipped with side ports for pressure monitoring and drug infusion and to allow introduction of the Doppler guide wire. Heart rate, aortic pressure,
coronary arterial pressure, and Q_{EMF} were monitored continuously.

After the shunt circuit was initiated, radiographic contrast material (Optiray-320, Mallinkrodt) was injected into the coronary cannula and a single-plane angiogram was recorded. Any small atrial or obtuse marginal branches arising from the proximal 2 cm of the LCx were identified and ligated to provide a nonbranching segment of artery distal to the tip of the cannula so that the flow rate in this segment was identical to that measured by the EMF. The distal 1 cm of the Doppler guide wire was shaped by hand into a curve to allow the wire to be steered within the coronary arterial tree. The guide wire was advanced through a side port into the main body of the cannula and into the LCx.

Flow to the LCx was varied by graded partial or total occlusion of the shunt circuit by a screw clamp, by reactive hyperemia after removal of the occlusion, and by injection of 8 mg of papaverine directly into the coronary cannula. Flows were systematically altered in this manner with the ultrasound transducer placed in each of three positions: within the cannula (1–2 cm from its tip), in the straight portion of the LCx more than 5 mm proximal to any branches, and in at least one position in a distal branch of the LCx. To test the effect of heart rate on the measurements, recordings were made at the spontaneous, unpaced heart rate and during atrial pacing at a rate of 150 beats per minute.

After each placement of the wire within the proximal LCx or a distal branch, while optimal velocity signals were being recorded, a single-plane cineangiogram of the vessel was obtained during injection of radiocontrast material (Figure 3).

At the end of each experiment, the dog was killed by intraventricular injection of potassium chloride.

**Quantitative Angiography**

Cineangiograms were used to determine the diameter and cross-sectional area of the vessels interrogated by the Doppler wire. With the silhouette of the steel cannula as a reference, the internal diameter of the vessel at the location of the sample volume (5 mm distal to the wire tip) was determined by the method of Brown et al.\(^{15}\) modified for single-plane images. Cross-sectional area was calculated by assuming a circular lumen.

**Analysis of Doppler Signals**

Doppler signals were analyzed on line by fast Fourier transform. The Doppler frequency shift spectrum was displayed as a scrolling gray scale, with the envelope of the spectrum corresponding to the instantaneous peak frequency shift. The instantaneous peak frequency shift was related to the instantaneous peak velocity by the Doppler equation:

$$\Delta f = \frac{2 f_v \cos \theta}{c}$$  \hspace{1cm} (1)

where \(\Delta f\) = Doppler peak frequency shift, \(f_v\) = transmission frequency (12 MHz), \(v\) = instantaneous peak velocity, \(\theta\) = angle of incidence of the beam to the blood stream (assumed to be 0°), and \(c\) = the speed of sound in blood (1,570 m/sec).

Doppler spectra generated on line by fast Fourier transform were recorded on videotape along with quadrature audio signals while simultaneous \(Q_{EMF}\) was recorded by computer. Only recordings made with stable wire position and with adequate angiograms for quantification were analyzed in detail. To minimize interference by low-frequency wall motion artifact and effects of uneven sampling of the flow profile, we chose to use the time average of the instantaneous spectral peak velocity (APV) for all calculations. APV was obtained by manual tracing of 2-second segments of the envelope of the phasic velocity spectrum on a computer bitpad. Positive and negative flow velocity envelopes were traced separately. A custom BASIC computer program calculated APV using the areas under the peak velocity curves and the time base of these measurements.

**Quantitative Flow Calculations**

We tested the ability of the Doppler guide wire to provide a quantitative estimation of flow rate in vessels and tubes of known diameter. We estimated mean velocity as 0.5×APV by assuming a time-average parabolic velocity profile across the vessel. Doppler-derived flow was calculated as
\[ Q_D = \frac{\pi D^2}{4} (0.5 \times \text{APV}) \]  

where \( Q_D \) = Doppler-derived time-average flow, \( D \) = vessel diameter, and \( \text{APV} \) = time average of the spectral peak velocity. For the in vitro experiments, \( D \) = measured internal diameter of the model tubes. For the animal studies, \( D \) = measured internal diameter of the coronary cannula or \( D \) = diameter of the proximal LCx measured by quantitative angiography at the location of the sample volume (5 mm distal to the guide wire tip).

**Statistical Analysis**

APV and \( Q_D \) were compared with \( Q_{EMF} \) and with the pulsatility index by use of linear regression, with calculation of \( r^2 \), slope, intercept, and SEE. ANCOVA was used to compare regression lines.
Results

In Vitro Experiments

The pulsatile flow provided by the roller pump in the five straight plastic tubes was varied from 0 to a maximum of 1,501 ml/min in the largest tube. Eight to 14 paired Doppler APV and QEMF measurements were made in each tube. In the four smaller tubes, APV measured by the Doppler guide wire was highly correlated with QEMF ($r^2=0.99$, 0.98, 0.99, and 0.99; SEE=1.31, 2.43, 1.10, and 1.18 for the tubes of 0.79, 1.59, 3.17, and 4.76-mm diameter, respectively) (Figure 4A). In the largest tube (7.94-mm diameter), the correlation between APV and QEMF was linear for flows up to 922 ml/min, with $r^2=0.99$ and SEE=0.82 calculated for nine points between 0 and 922 ml/min. At higher flows, the recorded APV fell below the line of regression for the lower flows.

When $Q_D$ was calculated for the five straight plastic tubes by Equation 2, estimating mean velocity as 0.5×APV, a very accurate estimate of QEMF was obtained for each of the four smaller tubes. The slope of the line of regression for $Q_D$ versus QEMF fell within the range of 1.00±0.04 in each case, with y intercepts within 5.6 ml/min of zero. In the 7.94-mm tube, $Q_D$ underestimated QEMF by approximately 20% at flows up to 922 ml/min and by larger amounts at flows between 922 and 1,501 ml/min. For the nine measurements made with QEMF from 0 to 922 ml/min, $Q_D=0.80(Q_{EMF})+7.10$ ml/min, $r^2=0.99$, and SEE=3.17 (Figures 4B and 4C).

Changing pulsatility in the straight 3.17-mm tube with constant QEMF had only minor effects on measured APV. Because QEMF was held constant while pulsatility was altered, measured APV would be expected to remain unchanged if pulsatility had no effect on Doppler measurements. At each of the three different mean flow rates, the APV recorded by the Doppler guide wire varied by no more than 10.4% from the expected APV for any measurement made over the range from nearly constant flow to the highest degree of pulsatility. (The “expected APV” at a given QEMF is defined as the average peak velocity that would occur if the flow profile were purely parabolic. Under this condition, the peak velocity is equal to twice the mean velocity. Expected APV could thus be calculated from QEMF and tube diameter by rearrangement of Equation 2 above.) We quantified the degree of pulsatility by deriving a “pulsatility index” calculated as maximum spectral peak velocity minus minimum spectral peak velocity divided by time-average spectral peak velocity (APV). Figure 5 displays the relation between measured APV and pulsatility at the three different values of QEMF. Although the differences between highest and lowest measured APV were small in all cases, linear regressions of APV versus pulsatility index at the three different flow rates were carried out to investigate whether any relation existed. This analysis produced inconsistent results. At the lowest flow rate, a statistically significant trend toward higher measured APV with increasing pulsatility was present ($r^2=0.80, p=0.007$). The reverse relation, i.e., lower measured APV with increasing pulsatility, was present at the middle flow rate, although this relation was of only borderline statistical significance ($r^2=0.57, p=0.051$). No relation was found at the highest flow rate ($r^2=0.01, p=0.97$). Even when statistically significant trends were present, the differences between the highest and lowest APV measured were small relative to the true velocity.
Tortuosity of the tube did have an effect on the measured flow velocity (Figure 6). The expected APV, calculated from $Q_{\text{EMF}}$, was consistently underestimated by 3–24% in the segments with radius of curvature of $\frac{1}{2}$ and $\frac{1}{4}$ in, regardless of direction of flow (positions 4, 5, and 6 in Figure 6A). Flow velocity measurements in the less tortuous portions of the model showed no systematic inaccuracies but did show moderate variability. There was still good linear tracking of changes in $Q_{\text{EMF}}$ by APV during a single placement of the wire, however. When $Q_{\text{EMF}}$ was varied between 0 and 183 ml/min with the sample volume in the tightest curve in the model (position 6 in Figure 6A, with wire and blood flow entering in the left-to-right direction), an excellent linear relation was found between APV and $Q_{\text{EMF}}$ ($r^2=0.99$). The slope of $Q_{D}$ versus $Q_{\text{EMF}}$ was 0.82 for the nine measurements made, representing a consistent underestimation of $Q_{\text{EMF}}$.

**In Vivo Experiments**

Under angiographic guidance, the Doppler guide wire was easily maneuvered within the main body of the coronary cannula and into the proximal and distal portions of the LCx (3.3–1.2-mm diameter) in all dogs. Doppler signals were stable, and signal quality remained unchanged for periods exceeding 30 minutes. Readjustment of the guide wire position was infrequently required. With a properly optimized wire position, signal-to-noise ratios of 20–30 dB (spectral peak signal level to spectral peak noise level) were typically measured, with good stability of the signals.

Representative tracings from the proximal and distal vessels are shown in Figure 7. In the cannula, only forward (positive) flow was seen. Both forward and reverse flow were clearly displayed in the proximal and distal vessels. In some positions in distal vessels, a high-amplitude, low-frequency signal was seen that was...
FIGURE 7. Representative phasic flow velocity spectra from one dog at baseline, during partial clamping of the perfusion circuit, and during reactive hyperemia. Top row: proximal left circumflex artery (LCx); diameter, 2.8 mm. Bottom row: Distal branch of LCx; diameter, 1.5 mm. Flow reversal is prominent in the distal vessel where it is not damped by extramural coronary capacitance.

typical of vessel wall motion artifact. This complicated the accurate identification of low-frequency forward or reverse systolic velocity components. However, this problem usually could be minimized by adjusting the position of the wire. Significant wall motion artifact was rarely encountered in proximal vessels and never in the cannula.

The flow to the LCx varied from 0 to 180 ml/min during clamping, reactive hyperemia, and papaverine injections. Eleven to 21 measurements were made at different flow rates during each placement of the guide wire. The APV displayed good linear correlation with QEMF. In the cannula, where one placement was made for each dog, \( r^2 \geq 0.99 \) and SEE = 0.85–1.49 for each placement. In the proximal LCx, stable placements during sinus rhythm with adequate angiograms for quantification were made at least two times in each dog. For the nine proximal LCx placements, \( r^2 \) ranged from 0.93 to 0.99 and SEE = 1.20–2.17. Figures 8A and 8B show representative relations from within the coronary cannula and proximal LCx. Seven different distal sites in small branches of the LCx systems were interrogated, their diameters ranging from 1.2 to 1.9 mm by quantitative angiography. In the distal vessels, the Doppler guide wire necessarily measured flow velocity in a vessel receiving only a portion of the entire LCx flow measured by the EMF. Despite this, the linear regression of APV versus QEMF in the distal vessels produced values of

FIGURE 8. Plots of linear regression of the time average of spectral peak velocity (APV) derived from the Doppler frequency shift vs. left circumflex artery blood flow determined by electromagnetic flowmeter (QEMF). One representative relation is shown for each of three transducer locations. Panel A: Coronary cannula. Panel B: Left circumflex artery proximal to any visible branches. Panel C: Distal obtuse marginal artery (1.5-mm diameter).
r² ranging from 0.86 to 0.99 and SEE from 0.77 to 1.76. Figure 8C shows the relation from one dog. Zero intercepts were small (0±4.4 cm/sec) relative to the range of velocities measured at all measurement sites in the cannula and proximal and distal vessels.

The calculation of Doppler-derived flow, QD, was highly predictive of QEMF for Doppler measurements obtained within the coronary cannula (QD=0.95 QEMF−4.37 ml/min, r²=0.99, and SEE=2.02 for all dogs combined) (Figure 9A). For individual dogs, r²≥0.99, and the slopes ranged from 0.86 to 0.99.

In the proximal LCx, QD remained highly predictive of QEMF, QD=0.85QEMF+1.70 ml/min, r²=0.94, and SEE=2.98 for all nine placements in the four dogs combined (Figure 9B). For individual placements, r² ranged from 0.93 to 0.99, with slopes ranging from 0.78 to 1.15.

Spontaneous heart rates ranged from 68 to 130 beats per minute during various interventions. Left atrial pacing at 150 beats per minute with the Doppler guide wire tip positioned in the proximal LCx did not appreciably alter the quality of signals in any dog. In one dog, second-degree atrioventricular block appeared below 150 beats per minute; this dog is excluded from analysis of the effect of heart rate on flow velocity measurement. Figure 10 shows linear regressions of APV versus QEMF for flow measurements in the proximal LCx in the remaining three dogs collected at baseline heart rate and during pacing at 150 beats per minute. ANCOVA revealed no significant difference between the slopes of the lines in any dog. The y intercepts of the lines were not significantly different in two dogs; a small but statistically significant difference in y intercept (+0.6 versus −4.4 cm/sec, p<0.05) was present in the third dog.

**Discussion**

**In Vitro Models**

Our in vitro experiments have shown that the Doppler guide wire linearly tracks changes in time-average rate of pulsatile blood flow through straight plastic tubes up to 4.76 mm (√6 in.) in diameter. QD, calculated using known tube diameters and estimating mean velocity as 0.5×APV, was nearly identical to QEMF over the range of flows tested in these small tubes. Properly calibrated EMFs are known to provide a very accurate measurement of true flow rate. The APV was therefore almost exactly twice the true mean velocity in this system composed of long, straight tubes of uniform diameter, in which the velocity profiles were expected to be parabolic. This suggests that the wire did not measurably alter the flow velocity profile within the sample volume. This represents a significant improvement over a 3F Doppler catheter with end-mounted, ring-shaped...
transducer. Tadaoka et al. have rigorously tested such a 3F Doppler catheter, manufactured by Millar Instruments, including a careful analysis of the effect of the catheter on the flow field in a model vessel. Using Reynolds numbers matched to those commonly found in the coronary circulation, they found a significant disturbance of flow extending well beyond the distance to which the sample volume could be placed from the catheter tip because of limitations of strength of the signal. In another in vitro model, they showed that the Millar catheter underestimated true flow velocity at all sample ranges because of depression of the peak flow velocity downstream from the catheter tip. The reduced size of the Doppler guide wire appears to result in significantly less flow disturbance than a 3F (1-mm-diameter) Doppler catheter.

In the largest tube used for our measurements, with a 7.94-mm- (3/16-in.)-diameter lumen and 60-cm entrance length, flow was consistently underestimated by about 20% at flows up to 922 ml/min. In this lower range, the underestimation may result from an inability to direct the wire far enough away from the wall to sample the central portion of the stream, so that the true peak velocity was not recorded. Also, the large tube diameter would have allowed significant deviation of the transducer on the curved wire tip from the direction of flow, contributing to further underestimation by increasing the angle between the ultrasound beam and the flow vector. At three flow rates above 922 ml/min, flow was underestimated by even more than 20%. To evaluate possible reasons for the worsened inaccuracy at high flow rates, the Reynolds numbers for the test conditions and the entrance length necessary for fully developed flow with parabolic flow profile were calculated. Reynolds number at the highest flow rate was 1,321. Although this is higher than Reynolds numbers typically present in the coronary circulation, it is not high enough to predict turbulent flow. Entrance length was calculated according to Caro et al. as

\[ X = 0.03 \frac{d}{(Re)} \]

where \( X \) = entrance length, \( d \) = diameter of a straight tube, \( Re \) = Reynolds number, and 0.03 = experimentally derived constant. The maximum entrance length necessary for fully developed flow under our conditions was 32 cm, which is shorter than the 60 cm we provided. Thus, neither turbulence nor inadequate entrance length would predict a nonparabolic flow profile at these flow rates. The observed inaccuracy may result from suboptimal positioning or instability of the wire tip under these high flow conditions.

The effects of changes in pulsatility of flow on the measured APV in our in vitro system were minor. Marked increases in pulsatility at three different constant flow rates resulted in a slight increase in measured APV at one Q\textsubscript{EMF}, a slight decrease of borderline statistical significance at another, and no change at the third. In no case did the measured APV differ from the expected APV by more than 10.4%, indicating that even exaggerated changes in pulsatility in a smooth, straight tube have at most a small effect on the measured APV. Whether these minor differences may be seriously amplified in tortuous and/or diseased human coronary arteries is unknown.

In the tightly curved portions of the tortuous tube, APV was lower than expected, probably because of a combination of deformed flow profiles in the tortuous segments and inability to direct the sample volume into the peak flow region. The wire tip was seen to “hug” the outer wall of the curved segments, even with a moderate curve introduced into the distal segment of the wire. Even though the relation between APV and Q\textsubscript{EMF} remained linear in a tightly curved segment, albeit with a slope representing a consistent underestimation in the true flow velocity, small changes in wire position in a tortuous vessel may produce significant differences in the measured APV.

**In Vivo Model**

The in vivo studies establish several potentially useful features of the new Doppler guide wire system.

1) The Doppler guide wire could be steered easily into proximal and distal branches of the coronary arterial tree. The flexibility and steerability of the angioplasty guide wire did not appear to be appreciably altered by the presence of the end-mounted crystal or its electrical wires, allowing the transducer to be delivered to very distal portions of the coronary system. Further evaluation in humans during PTCA will be needed to assess the handling characteristics of the Doppler guide wire in crossing stenoses and to explore its potential to serve both as a diagnostic device and as a guide for angioplasty balloon catheters during PTCA.

2) Phasic velocity recordings with a high signal-to-noise ratio were recorded for prolonged periods in proximal and distal vessels as small as 1.2 mm in diameter. The Doppler signal strength is dependent on the wire position relative to the flow stream within the vessel, and the wire must be manipulated to obtain the optimum signal at a given location. The small diameter of the Doppler guide wire minimizes the size of vessel it can enter without significantly affecting flow. With its cross-sectional area of only 0.164 mm\(^2\), the Doppler guide wire would cause a 15% area reduction of a circular lumen 1.2 mm in diameter. In contrast, a 1-mm-diameter catheter would occlude 69% of the area of a 1.2-mm-diameter circular lumen. Studying artificial stenoses 3 mm in length, Folts et al. found that maximal flow through a vessel is not decreased until 36\(\pm\)10% of the diameter (approximately 59% of the area) is occluded. The Doppler guide wire should make it possible to measure more accurately the actual phasic inflow to the myocardium in closed-chest humans by recording relatively undisturbed flow velocity patterns in small vessels distal to the major capacitance of the large extramural coronary arteries.

3) Forward and reverse flow were well separated. Although the problem of low-frequency wall motion artifact was occasionally encountered, especially at the onset of systole, this usually could be minimized by careful repositioning of the guide wire, allowing detailed recording of the low or negative flow velocities present during systole and low-flow states. The ability to measure both forward and reverse flow becomes critical in small vessels in which reverse flow from the myocardium may be markedly altered by changes in contractility, coronary perfusion pressure, and vasodilatation.
may be important in assessing the pathophysiological significance of coronary hemodynamic abnormalities.

4) In the in vivo experimental system used in this study, the Doppler guide wire linearly tracks changes in flow rate with good fidelity, and zero offsets are small. This consistent feature of ultrasonic Doppler devices6,11,12 provides the potential for evaluating interventions that affect mean flow rate, such as vasodilator drugs or angioplasty of a stenosed vessel. Good linear relations were demonstrated between APV and QEMF for measurements made within the rigid coronary cannula and in the proximal LCx. In the distal vessels, our experimental preparation did not allow us to obtain a measure of the flow rate in the individual branches of the LCx interrogated. We presumed that in a dog with normal coronary arteries, with no significant obstruction from the guide wire, the flow in a small branch would increase and decrease proportionally with flow in the entire LCx measured by the flowmeter at the entrance to the cannula. In distal branches as small as 1.2 mm, reasonably good linear correlations were in fact obtained between APV and QEMF. The correlations were lower, however, in the distal branches than in the proximal vessels. This may result from heterogeneity of flow or flow reserve in small regions of myocardium, from greater variation in small vessel diameter for different flow rates, or from wall motion artifact.

5) By estimating mean velocity as 0.5×time average of spectral peak velocity, a relatively accurate quantitative estimate of flow rate can be made in the models used in this study. Johnson et al8 demonstrated that spectral peak velocity is more accurate than zero crossing methods or spectral mean velocity when used to assess a coronary stenosis using a 3F Millar Doppler catheter with end-mounted transducer. Zero crossing and spectral mean velocity measurements may be more sensitive to low-frequency wall motion artifact and to uneven sampling of the velocity profile across a vessel. The divergent beam generated by the Doppler guide wire increases the likelihood that a true peak velocity will be accurately detected, because part of the relatively large sample volume is likely to contain the portion of the flow stream moving at peak velocity when signal strength is optimized. The ability to quantify flow rate is less critical to most uses of intracoronary Doppler than is the consistent linear tracking of changes in flow velocity. It may be useful for some specific applications, however, especially where significant changes in vessel size may occur, such as before and after PTCA with large differences in distending pressure of distal vessels.

6) The flow velocity signals of the Doppler guide wire system were not importantly affected by increasing the heart rate to 150 beats per minute in our in vivo preparation. Increased heart rate would be expected to increase the motion of the heart and the rate of change of flow velocity. It would have only a minor effect on the pulsatility of flow, however (defined as maximum minus minimum flow velocity divided by average velocity). Effects of pulsatility changes per se were examined using the in vitro system only. In our in vivo pacing experiments, the relations between APV and QEMF at spontaneous heart rates and at 150 beats per minute were superimposable except for a difference in zero intercept of 5.0 cm/sec in one dog. This difference may reflect zero drift in the EMF or may be a function of the Doppler device. Though it reached statistical significance, differences of this magnitude (which represents a difference of 21 ml/min in flow) are likely to be of only modest clinical importance. The frequency response of the spectrum analyzer (which calculated approximately 90 spectra per second) is fast enough and the signal-to-noise ratio (typically >20 dB for a properly optimized wire position) is high enough that rapidly changing phasic flow velocities at high heart rates are faithfully recorded. The Doppler guide wire may be useful in clinical studies during spontaneous tachycardia or for evaluating a coronary stenosis by means of rapid pacing.

**Limitations**

Although the Doppler guide wire appears to overcome some of the specific limitations of other intravascular Doppler devices, the new device and the validating studies reported here have some important limitations of their own that deserve to be emphasized.

1) The floppy angioplasty guide wire that delivers the ultrasound transducer is relatively fragile and may be damaged by rough handling inside or outside the coronary system.

2) The quality of the signal and the value of the peak velocity detected are critically dependent on consistent and careful positioning of the wire. Each placement of the wire requires optimization of the signal strength by manipulation of the wire to maximize the likelihood that the true peak of the velocity profile is included. The comparability of two measurements made at different times may suffer if the wire position differs. This will be especially true in large vessels, tortuous segments, and regions with varying luminal dimensions or configurations.

3) The effects of alterations in pulsatility have been systematically studied only in a straight, smooth tube. Although only minor effects on the measured APV were found in our experiment, we did not accurately reproduce the conditions likely to be encountered clinically. During coronary angioplasty or other interventions involving transient occlusion of coronary flow, marked alterations in the pulsatility of coronary flow may be encountered because of variations in myocardial contractility. These alterations may have a greater effect on Doppler measurements in tortuous and irregular arteries than in a straight plastic tube; this possibility must be investigated before these results may be confidently extrapolated to a clinical setting.

4) Our method of calculating flow using APV is susceptible to several potential sources of inaccuracy. It depends on the assumptions that a time-average parabolic flow velocity profile occurs in which peak velocity is twice the mean velocity, that the peak of the flow velocity profile remains within the transducer’s sample volume throughout the cardiac cycle, and that the flow velocity profile remains unchanged with changes in the flow rate. Normal proximal coronary arteries have been shown to have variable flow velocity profiles, the shapes of which may be almost perfectly parabolic, skewed toward the inner or outer wall, or trapezoidal.3,19–21 Near branches and in vessels that are tortuous or have intimal irregularities or stenoses, there is significant flow separation and deformation of the flow field.3,22 The long, unbranched coronary cannula in our canine prep-
Table 1. System Specifications

<table>
<thead>
<tr>
<th></th>
<th>Prototype system</th>
<th>Production system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler type</td>
<td>Pulsed</td>
<td>Pulsed</td>
</tr>
<tr>
<td>Doppler frequency</td>
<td>12 MHz</td>
<td>12 MHz</td>
</tr>
<tr>
<td>Pulse repetition rate</td>
<td>13.3–100 kHz</td>
<td>12–96 kHz</td>
</tr>
<tr>
<td>Transmit repetition length</td>
<td>0.17–2.0 μsec</td>
<td>1.0 μsec</td>
</tr>
<tr>
<td>Range gate delay</td>
<td>3.0–32.5 μsec (2.4–25.5 mm)</td>
<td>3.3–20.0 μsec (2.6–15.6 mm)</td>
</tr>
<tr>
<td>Range gate width</td>
<td>0.4–4.3 μsec</td>
<td>1.0 μsec</td>
</tr>
<tr>
<td>Display type</td>
<td>Scrolling spectrum</td>
<td>Scrolling spectrum plus two physiological traces</td>
</tr>
<tr>
<td>Display dynamic range</td>
<td>0–60 dB</td>
<td>0–64 dB</td>
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<tr>
<td>Spectrum analyzer input</td>
<td>48 dB</td>
<td>72 dB</td>
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<tr>
<td>Fourier transform rate</td>
<td>=90 spectra/sec</td>
<td>100 spectra/sec</td>
</tr>
<tr>
<td>Sweep speed</td>
<td>2.2 sec/screen</td>
<td>1.6, 2.4, or 4.8 sec/screen</td>
</tr>
<tr>
<td>Full-scale velocity range</td>
<td>17–200 cm/sec (8 ranges)</td>
<td>45–500 cm/sec (8 ranges)</td>
</tr>
<tr>
<td>Positive velocity range</td>
<td>80% of full scale</td>
<td>60–90% of full scale</td>
</tr>
<tr>
<td>Doppler direction</td>
<td>Selectable</td>
<td>Selectable</td>
</tr>
<tr>
<td>Spectral peak velocity estimation</td>
<td>Off-line manual digitization</td>
<td>Computerized tracking with real-time display</td>
</tr>
<tr>
<td>Calculations</td>
<td>Off-line program calculates APV, other parameters</td>
<td>On-line computation of APV, other parameters</td>
</tr>
<tr>
<td>Numerical outputs</td>
<td>None</td>
<td>Phasic and mean (APV) of spectral peak velocity</td>
</tr>
<tr>
<td>General description</td>
<td>Custom pulsed Doppler instrument, spectrum analyzer, VCR, video printer, computer</td>
<td>Cardiometrics Model 5500: pulsed Doppler circuitry, spectrum analyzer, video display, VCR, and video printer</td>
</tr>
</tbody>
</table>

APV, time average of instantaneous spectral peak velocity; VCR, videocassette recorder.

aration may have allowed a more parabolic flow velocity profile to develop in the proximal LCx than is normally found in native coronary vessels and may have produced better correlations between QD and Q_{EMF} than would be found in uninstrumented vessels. In irregular, branched, or ectatic vessels, the relation between peak and mean velocity is likely to be even more inconsistent. This may limit the usefulness of quantitative flow calculations based on APV, especially in patients with diffuse coronary disease.

5) Inaccuracies in determination of the vessel cross-sectional area may also contribute to the variability of flow calculations. Our animal laboratory is equipped with only a single-plane cineangiographic system, and the extracorporeal shunt circuit precluded repositioning the dog to obtain orthogonal views for quantitative biplane angiographic assessment of the vessels. We did not detect any coronary arterial abnormalities by angiography in any of the dogs. For these normal coronary arteries, we assumed that cross-sectional area estimates based on a single diameter would be accurate. Nevertheless, inaccuracies in our estimations of vessel cross-sectional area may have occurred, and similar inaccuracies may limit the reliability of clinical measurements.

Conclusions

The new Doppler guide wire provides detailed phasic flow velocity spectra from small coronary vessels and linearly tracks changes in mean flow rate under a variety of experimental conditions. A proposed application of the device for quantitative estimation of volume flow appears feasible in the experimental models we have used but may prove to be less accurate in patients with diseased coronary arteries. Compared with 1-mm Doppler catheters, the Doppler guide wire causes less disruption of flow velocity profiles and is less obstructive in very small arteries. The new device may prove simpler to use during cardiac catheterization and angioplasty by serving as a PTCA guide wire as well as a diagnostic device. Phenomena thus far studied only in laboratory animals or in open-chest humans may become accessible in the human cardiac catheterization laboratory with the Doppler guide wire. Among these are measurement of changing systolic:diastolic flow velocity ratios in the poststenotic segment after relief of a stenosis3 and the detailed analysis of the true phasic inflow to the myocardium in distal vessels.23 Flow patterns in small coronary veins may also be accessible by retrograde catheterization via the coronary sinus. Study of phasic flow velocity measurements performed in small coronary vessels may lead to improved understanding of the pathophysiology of coronary artery disease and other cardiac diseases as well as the effects of therapeutic interventions.

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Appendix

System Specifications

The prototype Doppler system used for this study consisted of a custom Doppler instrument built by Cardiometrics, Inc. connected to a Medasonic SP-25A spectrum analyzer, a VHS video cassette recorder, a video page printer, and a computer. The computer was used for data acquisition and to control the operation of the Doppler instrument. The Doppler instrument could be programmed for a wide range of parameters; the values used for this study are reported in the text. This prototype system has been replaced by a production version (Cardiometrics FloMap®, model 5500) that incorporates all the capabilities of the original prototype system and is being used for ongoing research and clinical studies with the Doppler guide wire. The specifications for the production system are included in Table 1 for reference.

References

Validation of a Doppler guide wire for intravascular measurement of coronary artery flow velocity.
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