Analysis of pulsatile coronary pressure and flow velocity: looking beyond means

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Chapter 4

Applicability of local arterial wave speed assessed by single-point method in healthy and diseased human coronary vessels

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Submitted
Abstract

**Background:** A novel single-point technique has recently been presented to calculate an index of local wave speed (c) in human coronary arteries, but its applicability has not yet been tested in diseased vessels. Wave speed is needed to separate forward and backward travelling components in wave intensity (WI) analysis.

**Methods:** In 29 patients distal intracoronary pressure (Pd) and Doppler velocity (v) were recorded at rest and during hyperemia in a normal reference vessel and in a diseased vessel before and after revascularization. Large vessel tone was minimized with nitroglycerine. Microvascular resistance (MR) and c were calculated from Pd and v. For 3 subjects, the area under separated WI waveforms was determined for a range of c from 25% to 200% of its calculated value.

**Results:** In the presence of a stenosis, microvascular vasodilation by adenosine decreased Pd by 20 mm Hg (P<0.0001) and c from 34.4 ± 18.2 to 27.5 ± 13.4 m/s (P<0.001). Stent placement reduced hyperemic MR by 26% (P<0.005) and increased Pd by 26 mm Hg (P<0.0001), but paradoxically further decreased c to 13.1 ± 7.7 m/s (P<0.0001). Changes in c correlated strongly with changes in MR (P<0.001). Varying c from -50% to +100% of the calculated value did not substantially alter separated WI, but a deviation of -75% introduced marked changes.

**Conclusions:** Local coronary wave speed derived from the single-point method is influenced by distal microcirculation and proximal stenosis, thereby limiting its application in studying physiological responses. However, this parameter is still applicable for wave separation in coronary WI analysis.
Introduction

Arterial wave speed is an important physiological marker of cardiovascular risk [2, 16, 24] which results from its inverse relation to vessel wall distensibility. Consequently, wave speed is influenced by factors that affect wall stiffness, such as age, vascular disease, distending pressure and vascular tone [2, 10, 12, 14, 22]. It is also a fundamental parameter required in wave intensity analysis (WIA) for the separation of traveling waves into their forward and backward components [6, 15, 25].

Wave speed in the human peripheral arteries can be measured using the foot-to-foot method [11] or the pressure-velocity (PU) loop method [7, 8, 25]. The foot-to-foot method involves simultaneous pressure recordings at two locations with a known distance apart and derivation of the time it takes the wave to travel that distance. This technique yields the average wave speed between the two measuring points and therefore must be applied to vessel segments with fairly uniform wall properties. The PU-loop method involves simultaneous pressure and velocity recordings at a single location within a vessel. Local wave speed is then derived from the slope of the linear portion of the pressure-velocity loop. This linear portion must correspond to the period when only unidirectional waves are present in the system [6].

Both methods are, however, unsuited to determine wave speed in human coronary arteries. The coronary vessels are too short and tortuous to apply the foot-to-foot method. On the other hand, because coronary waves are generated simultaneously from proximal and distal sources, there is no period during the heart cycle when only forward or only backward waves are present [3] and therefore the PU-loop method cannot be used either.

Recently, Davies et al. [4] presented a new single-point technique for local wave speed calculation that uses complete heart cycles without restrictions about wave travel direction. Application of this technique in healthy human coronary vessels at resting flow conditions demonstrated good correlations between coronary and aortic wave speed. Furthermore, coronary wave speed increased with age and decreased substantially after pharmacological reduction of epicardial vessel tone. The authors therefore concluded that this method is suitable for implementation in human coronary arteries [4]. However, the applicability of this promising single-point technique has not yet been investigated for conditions frequently encountered in clinical practice. Diseased coronary vessels may introduce additional localized reflection sites that may render this method less accurate. Similarly, the potential influence of clinical procedures that alter coronary distending pressure has also not been studied.

The aims of this study were to investigate 1) to what extent local wave speed in human coronary arteries as derived from the single-point technique differs between healthy and diseased vessels and 2) how it is affected by altered distending pressure due to microvascular vasodilation and revascularization of an epicardial stenosis. Since wave speed is needed for wave separation in WIA we also tested the sensitivity of wave separation to deviations from the calculated wave speed.
Methods

Study population

The study group consisted of 29 subjects (mean age 59 ± 9 yrs, 23 males) with stable angina pectoris who were scheduled for elective balloon angioplasty and stent placement. All patients had at least one angiographically normal vessel (<30% diameter stenosis) and one vessel with a single de novo lesion. Exclusion criteria included prior coronary intervention, recent myocardial infarction, cardiomyopathies, valvular disease and the presence of visible collaterals. The protocol was approved by the medical ethics committee of our institution and all patients gave written informed consent.

Medication and protocol

All patients continued their prescribed antianginal and antiplatelet medication. Cardiac catheterization was performed by the femoral approach using a 5F or 6F guiding catheter. An intracoronary bolus of 0.1 mg nitroglycerin was given at the beginning of the procedure and was repeated every 30 min thereafter to minimize large vessel tone throughout the protocol. Hemodynamic measurements were obtained in an angiographically normal reference vessel and in the diseased vessel before and after revascularization by stent placement. Data for each condition were collected continuously at rest and throughout the hyperemic response to a 20-40 μg, i.e. bolus of adenosine.

Hemodynamic measurements

Aortic pressure (P_a) was measured via the guiding catheter at the coronary ostium. A 0.014-inch dual-sensor guidewire (Volcano Corp., Rancho Cordova, CA) was advanced to a distal position in the interrogated coronary vessel to record intracoronary perfusion pressure (P_d) and flow velocity (v) signals [19, 23]. The Doppler sensor was located at the tip and the pressure sensor 3 cm proximal to the tip. Care was taken to place the sensors in a smooth vessel segment without geometric discontinuities and to obtain an optimal and stable velocity signal. Sensor position was maintained before and after stent placement. After processing by the respective instrument consoles (WaveMap and FloMap, Volcano Corp.), the hemodynamic signals and ECG were digitized at 120 Hz for off-line analysis.

Data analysis

Data processing was performed using custom software written in Delphi (version 6.0, Borland Software Corporation, Cupertino, CA). Smoothed derivatives of the P_d and v signals were obtained by the Savitzky-Golay convolution method using an 11-point third order polynomial filter [18]. Based on the ECG R-peak of selected consecutive heart beats, average P_a, P_d, v, and HR were calculated during resting and peak hyperemic flow conditions over 8-9 and 2-3 cycles, respectively. A corresponding velocity-based index of microvascular resistance was derived as MR = P_d/v [19, 23]. The local coronary wave speed c was obtained as [4]
Wave speed in healthy and diseased coronary vessels

\[ c = \frac{1}{\rho} \sqrt{\frac{\sum dP_d^2}{\sum dv^2}} \]  

(4.1)

where \( dP_d \) and \( dv \) are the distal pressure and velocity differentials between successive sampling points and the summations were taken over consecutive heart cycles during resting and hyperemic flow periods. A value of \( \rho = 1050 \) kg/m\(^3\) was used for blood density.

The sensitivity of separated waves in WIA to changes in local conditions was examined for examples of 3 patients with different wave speeds. For each condition, separated forward and backward wave intensity (WI) was calculated for ensemble averaged cycles according to [3]:

\[ WI = \frac{1}{4pc} \left( \frac{dP_d}{dt} \pm \rho c \frac{dv}{dt} \right)^2 \]  

(4.2)

Note that this derivative calculation yields a wave intensity that is independent of the sampling rate. The ratio of the respective sums of all forward and backward wave energies was calculated to test whether integrated forward and backward waves cancel without summation of energy from one heart cycle to the next which is one of the assumptions underlying the derivation of the single-point wave speed equation [4].

The extent to which the integrated forward and backward wave energies depended on wave speed was tested for hyperemic data obtained in three patients in the reference vessel and in the diseased vessel before and after stent placement by varying wave speed from 25% to 200% of the corresponding actual value assessed from the single-point technique.

**Statistical analysis**

Data are expressed as mean ± SD. Hemodynamic data between different steps of the protocol were compared using analysis of variance with repeated measures, followed by contrast analysis (SPSS, version 12.0). Results obtained for resting and hyperemic conditions at each step of the protocol were compared using Student’s paired \( t \)-test. Linear regression analysis was used to investigate relations between continuous parameters. Statistical significance was assumed at \( P<0.05 \).

**Results**

Distal coronary artery measurements were obtained in all 29 patients before and after stent placement. Mean diameter stenosis was 55.7 ± 11.4%. Suitable measurements in the reference vessel were not available in six patients. Stenotic lesions were predominantly located in the left anterior descending artery (n = 19), while most reference vessels were the circumflex coronary artery (n = 19).

A typical measurement sequence obtained in a reference vessel is depicted in Figure 4.1. The aortic pressure signal shows two short periods where adenosine was injected into the coronaries and the catheter was flushed. The subsequent vasodilation is apparent from the flow velocity increase in the top panel. The distal
coronary pressure, \( P_d \), in the second panel from the top is hardly affected by the adenosine injection. The beat-averaged microvascular resistance decreased by a factor of three and the calculated wave speed fell concomitantly by a factor of two.

![Figure 4.1: Response to vasodilation by adenosine recorded in a reference vessel. Tracings show continuous recordings of distal velocity \( v \) and pressure \( P_d \), aortic pressure \( P_a \) and ECG. Per-beat values of microvascular resistance (MR) and wave speed \( c \) are displayed in the two lower panels. Adenosine is injected between \( t = 7s \) and \( t = 12s \). Vasodilation of the microcirculation has an immediate and prominent effect on wave speed.](image)

**Table 4.1: Hemodynamic values and wave speed at baseline and during hyperemia**

<table>
<thead>
<tr>
<th></th>
<th>stenosis ( (n = 29) )</th>
<th>stent ( (n = 29) )</th>
<th>reference ( (n = 23) )</th>
</tr>
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<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>71 ± 13</td>
<td>71 ± 15</td>
<td>67 ± 13</td>
</tr>
<tr>
<td>( P_a ) (mm Hg)</td>
<td>103 ± 15</td>
<td>104 ± 16</td>
<td>103 ± 15</td>
</tr>
<tr>
<td>( P_d ) (mm Hg)</td>
<td>82 ± 19</td>
<td>101 ± 15( ^\dagger )</td>
<td>100 ± 15( ^\ddagger )</td>
</tr>
<tr>
<td>( v ) (cm/s)</td>
<td>16 ± 6.7</td>
<td>19.0 ± 6.1( ^\dagger )</td>
<td>19.6 ± 7.5</td>
</tr>
<tr>
<td>MR (mm Hg/cm/s)</td>
<td>5.90 ± 2.70</td>
<td>5.93 ± 2.39</td>
<td>5.79 ± 1.99</td>
</tr>
<tr>
<td>( c ) (m/s)</td>
<td>34.4 ± 18.2</td>
<td>25.0 ± 14.6( ^\dagger )</td>
<td>21.5 ± 8.0( ^\ddagger )</td>
</tr>
<tr>
<td><strong>Hyperemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>71 ± 13</td>
<td>70 ± 13</td>
<td>68 ± 12</td>
</tr>
<tr>
<td>( P_a ) (mm Hg)</td>
<td>99 ± 15( ^\ddagger )</td>
<td>97 ± 14</td>
<td>97 ± 15( ^* )</td>
</tr>
<tr>
<td>( P_d ) (mm Hg)</td>
<td>61 ± 16( ^* )</td>
<td>87 ± 14( ^\dagger )</td>
<td>94 ± 14( ^\ddagger )</td>
</tr>
<tr>
<td>( v ) (cm/s)</td>
<td>30.1 ± 15.7( ^* )</td>
<td>58.1 ± 16.9( ^\dagger )</td>
<td>54.9 ± 16.9( ^\ddagger )</td>
</tr>
<tr>
<td>MR (mm Hg/cm/s)</td>
<td>2.53 ± 1.25( ^* )</td>
<td>1.67 ± 0.73( ^\dagger )</td>
<td>1.82 ± 0.44( ^\ddagger )</td>
</tr>
<tr>
<td>( c ) (m/s)</td>
<td>27.5 ± 13.4( ^* )</td>
<td>13.1 ± 7.7( ^\dagger )</td>
<td>10.5 ± 4.1( ^\ddagger )</td>
</tr>
</tbody>
</table>

\( ^* P<0.001 \) compared to baseline; \( ^\dagger P<0.05 \) compared to previous step; \( ^\ddagger P<0.05 \) reference compared to stenotic vessel.
Effect of distal vasodilation and revascularization

Average hemodynamic and wave speed data are summarized in Table 4.1 for all three steps of the protocol. Heart rate did not change throughout the procedure. Mean aortic pressure was 103 ± 15 mm Hg at rest and decreased slightly during hyperemia, while coronary flow velocity increased substantially (P<0.0001).

The effect of age on local wave speed is depicted in Figure 4.2 at rest (A) and during hyperemia (B) for the reference vessel as well as the target vessel before and after stent placement. There was a significant positive relation between local coronary wave speed and age at rest for all vessel conditions. After vasodilation, significant age-dependency was only maintained for the undiseased reference vessel. The slopes of the regression lines were not significantly different between vessel conditions or between rest and vasodilation.

Figure 4.2: Relation between coronary wave speed and age at rest (A) and during hyperemia (B). There was no significant difference in the slopes of the regression lines between healthy, treated and diseased vessels or between resting and hyperemic conditions.
Figure 4.3 illustrates changes in distal coronary pressure and wave speed induced by hyperemia and stent placement. Coronary wave speed decreased after microvascular vasodilation in all conditions ($P<0.001$). Both at rest and during hyperemia, local wave speed was substantially higher in the presence of a proximal stenosis than after revascularization or in the reference vessel ($P<0.005$): distal to the stenosis, $c$ decreased from $34.4 \pm 18.2$ m/s at rest to $27.5 \pm 13.4$ m/s at hyperemia, while after revascularization $c$ decreased from $25.0 \pm 14.6$ m/s at rest to $13.1 \pm 7.7$ m/s at hyperemia.

![Figure 4.3: Changes induced in coronary wave speed and distal coronary pressure by microvascular vasodilation and stent placement. Open symbols refer to resting and closed symbols to hyperemic conditions. The error bars represent standard error of the mean. Symbols for statistical significance refer to wave speed: *$P<0.001$ compared to rest, †$P<0.005$ compared to the previous step, ‡$P<0.005$ reference compared to stenosis.](image)

Corresponding relative changes are shown in Figure 4.4. Hyperemia induced by microvascular vasodilation (left panels) reduced MR by $64 \pm 13\%$ averaged over all vessel conditions ($P<0.0001$). This was associated with a reduction in distal pressure by $20 \pm 9$ mm Hg with stenosis present, and by $14 \pm 11$ mm Hg and $7 \pm 5$ mm Hg after revascularization and in the reference vessel, respectively (all $P<0.0001$). Despite the larger drop in distal distending pressure in the presence of a stenosis, local wave speed decreased by the smallest amount in this condition: wave speed declined by $6.9 \pm 9.6$ m/s (17%) in the presence of the stenosis ($P<0.001$) compared to $11.8 \pm 10.9$ m/s (42%) in the treated and $10.9 \pm 5.9$ m/s (49%) in the reference vessel (both $P<0.0001$). Revascularization (right panels) lowered hyperemic MR by $26 \pm 28\%$ ($P<0.005$), while basal MR remained unchanged. Stent placement restored distal coronary pressure ($P<0.0001$) close to reference levels, but this increase in distending pressure was concomitant with a paradoxical decrease in wave speed: local wave speed fell by $9.4 \pm 14.3$ m/s (18%) at resting conditions ($P<0.005$) and by $14.3 \pm 12.9$ m/s (43%) during hyperemia ($P<0.0001$).
Figure 4.4: Relative changes in distal pressure, MR and wave speed due to distal vasodilation (A) and proximal stent placement (B). Local wave speed decreased despite an increase in distal pressure after revascularization. The error bars represent standard error of the mean. *$P<0.005$ compared to rest, †$P<0.05$ compared to the previous step, ‡$P<0.005$ reference compared to stenosis.

Figure 4.5 depicts the relationships between changes in wave speed and changes in MR and $P_d$. The decrease in wave speed induced by adenosine vasodilation (top panels) was positively correlated with the corresponding reduction in MR (top left panel) both in the reference and the stented vessel ($r = 0.46$, $P<0.03$ and $r = 0.69$, $P<0.0001$, respectively), but not in the stenotic vessel ($r = 0.29$, $P = 0.13$). Although the hyperemia-induced decrease in distending pressure was in general associated with a decrease in wave speed, no significant linear relation could be found between $\Delta c$ and $\Delta P_d$ for either of the vessel conditions (top right panel). Similar to the findings after vasodilation, stent placement (Figure 4.5 bottom panels) resulted in significant positive correlations between $\Delta c$ and $\Delta MR$ (lower left panel) for both resting ($r = 0.58$, $P<0.001$) and hyperemic ($r = 0.61$, $P<0.001$) conditions. In contrast, the increase in distending pressure after revascularization was associated with an unexpected paradoxical decrease in local wave speed (lower right panel), with a significant negative correlation between $\Delta c$ and $\Delta P_d$ at hyperemia ($r = 0.48$, $P<0.01$).
A  Effect of Vasodilation

![Graph A](image)

B  Effect of Revascularization

![Graph B](image)

**Figure 4.5:** Relationship of changes in wave speed with the associated changes in MR and distal coronary pressure. Changes in wave speed induced by vasodilatation (A) were positively correlated with changes in MR (left), but not with changes in coronary pressure (right). In contrast, changes due to stent placement (B) were positively correlated to changes in MR (left), but there was a negative correlation between changes in wave speed and changes in distal pressure (right).

**Effect of variations in c on separated wave intensity**

Figure 4.6 shows the effect of varying wave speed from one half to twice its calculated value on separated forward and backward wave intensity (WI) for examples of a diseased (top) and a reference vessel (bottom) from the same patient. Wave intensities are shown for a single ensemble-averaged heart cycle, during
hyperemia, starting with the R-peak of the ECG. The separated waves resulting from application of the calculated wave speed (Eq.4.1) are shown with grey filled areas. No additional self-canceling waves were induced nor was the WI profile or timing during the heart cycle substantially altered when $c$ deviated in a positive direction. Lowering $c$ had a larger influence on the separated waves.

![Stenosis and Reference Wave Intensity Graphs](image)

**Figure 4.6:** Separated forward and backward wave intensity (WI) from the diseased right coronary artery (62% diameter stenosis) (top) and the healthy left anterior descending coronary artery (bottom) of a 62 yr old patient. Separated WI is displayed for the value calculated with the single-point technique and variations of $c$ of -50%, +50% and +100% of this value. The ensemble-averaged beat starts with the R-peak of the ECG.

In order to quantify these changes in WI, we determined the integrated backward and forward wave area, representing the total energy during a complete heart cycle carried by backward and forward waves, respectively, and their ratio (B/F ratio). Results are shown in Figure 4.7 for three patients with calculated wave speeds.
between 21 and 57 m/s in the diseased vessel at hyperemia. For wave speed variations within ± 25%, the increase in forward wave area was on average not higher than 5.5% and the increase in backward wave area was lower than 3.5%. This led to a change in B/F that was 2.3% in the stenotic vessel, 0.4% after revascularization, and 0.5% in the reference vessel. These examples also illustrate that the B/F ratio (bottom panels) was closer to unity after stent placement and in the reference vessel than in the stenotic vessel. Variations in $c$ affected the B/F ratios to a larger extent the more they differed from unity at the calculated wave speed.

Figure 4.7: Total wave energy carried during the heart cycle by forward (F, top panels) and backward traveling waves (B, middle panels), and their ratio (B/F, bottom panels). Results during hyperemia are shown for different percent deviations from the wave speed calculated with the single-point technique. The selected examples from three patients cover different wave speeds (indicated in B/F panels), percent diameter stenoses and vessels. Separated wave energies markedly increase when a wave speed less than half of the calculated value is used. The B/F ratio is closer to unity in the absence of a stenosis.
Discussion

The results of this study show that local coronary wave speed as derived with the single-point technique [4] from epicardial hemodynamic measurements, is influenced by the presence of a stenosis and by alterations in downstream microvascular tone. Contrary to arterial wave speed behavior determined by other methods, the single-point measurement in coronary vessels did not correlate with changes in distending pressure in the expected positive way: 1) This paradoxical behavior was especially obvious when distending pressure was raised by revascularization and local wave speed decreased instead of increased. 2) In the presence of a proximal stenosis, wave speed measured at a distal location was not related to a decrease in distending pressure, but to a decrease in microvascular resistance. These two observations suggest that the assumptions underlying the derivation of wave speed by the single-point technique may not be met in diseased vessels and are likely to result in an inaccurate estimate of coronary wave speed. However, even considerable changes in wave speed values did not strongly affect the magnitude of separated wave intensities.

Coronary wave speed in normal and diseased vessels

The wave speed of 21.5 m/s we determined in reference vessels at rest compares favorably with the value of 20.4 m/s reported for healthy human coronary vessels [4]. It should be noted that our data were obtained after reducing conduit vessel tone by administration of nitroglycerin (0.1 mg i.c.) while those of Davies et al. [4] were determined in the absence of vasoactive drugs. Moreover, when in the study of Davies et al. 1 mg of intracoronary isosorbide dinitrate was given, wave speed dropped to 9.3 m/s, close to the value of 10.5 m/s that we obtained at full arteriolar vasodilation with adenosine [21]. It is not unlikely that this dose of isosorbide dinitrate induced a drop in perfusion pressure as well as transients in microvascular resistance during the 1-min measurement period. However, no data on coronary pressure or microvascular resistance were given in that study to test this possible explanation.

Animal studies on coronary wave speed [1, 17] report values in the order of 10 m/s for healthy vessels at resting conditions, which seems low compared to our values at rest for the reference vessel. Assuming that coronary can be correctly determined by the single-point method, two possible explanations for this difference should be considered. In the first place the relative age of the animals was likely lower and secondly, anesthesia-related reduced systemic pressures and/or microvascular dilation may have been present.

To the best of our knowledge this is the first study to report on coronary wave speed after full vasodilation and in diseased human coronary vessels. For rational assessment of our findings we therefore depend on internal consistency of our data. At rest we found a local wave speed of 34.4 m/s in an angiographically normal vessel segment downstream of a stenosis. This higher value of wave speed at a lower distending pressure than in the reference vessel could be indicative of a stiffer and diseased vessel wall. However, it is improbable that the wall properties downstream of the stenosis were affected by the (upstream) stent placement, yet, local wave speed dropped to the value in the reference vessel after revascularization. It is therefore unlikely that the higher wave speed distal to a stenosis as assessed with the single-point method reflects only local wall properties. On the other hand, the observed
effect of age on coronary wave speed is consistent with the generally accepted concept of an age-dependent increase in wall stiffness [9]. Hence the single-point wave speed is certainly influenced by vessel wall properties but not solely.

**Relationship between \( c \), intraluminal pressure and downstream microvascular conditions**

Wave speed in arteries is directly linked to distending pressure and elastic properties of the vessel wall [1, 5]. From the data shown in Figure 4.3 it is apparent that both wave speed and distal perfusion pressure decreased with vasodilation. However, they changed in opposite directions after revascularization of a proximal stenosis, when local coronary wave speed declined despite the increase in distending pressure.

The absence of a relation between changes in wave speed and distending pressure became more apparent when we examined individual patient data. The decrease in \( c \) induced by vasodilation was not related to changes in \( P_d \) (Figure 4.5, top right) and there was a paradoxical inverse correlation between changes in \( c \) and \( P_d \) after stent placement (Figure 4.5, bottom right). In contrast, we found that changes in \( c \) induced either by vasodilation or by angioplasty were positively related to changes in MR (Figure 4.5, left panels).

We believe that our observations clearly indicate that epicardial wave speed as derived from the single-point technique is influenced by changes in distal microvascular resistance. Davies et al. [4] briefly discussed this possibility but concluded that this was unlikely because they found similar wave speeds in different coronary vessels. However, our observations demonstrate that perfusion conditions of the downstream vascular bed can affect wave speed derived from the single-point method.

**Assumptions of the single-point technique**

One of the assumptions for the application of the wave speed single-point technique is that there is no summation of energy from one heart cycle to the next [4], i.e., \( B/F = 1 \). We demonstrated in Figure 4.7 for 3 patients that, although this assumption is roughly fulfilled in the reference and the treated vessel, it does not hold in the presence of a stenosis proximal to the measurement location. This observation suggests that a crucial prerequisite for the application of the single-point technique is not satisfied in diseased coronary arteries, and that the wave speed values calculated in these vessels may not be accurate. Further, the formula given in Eq. 1 was derived based on minimization of total wave intensity over complete heart cycles [4] since an incorrect wave speed would generate self-canceling artifacts in the calculation of separated forward and backward wave intensity. However, as discussed by the authors [4], local reflection sites generate real forward and backward waves which would not necessarily cancel each other out. Since a stenosis basically represents a proximal reflection site for our distal measurements [13, 20], this could provide an explanation for the unusually high wave speeds we obtained in angiographically normal vessel segment distal to a stenosis.

Possible reflections from the stent do not seem to affect the single-point technique, because the \( c \) values we calculated after revascularization both at resting and hyperemic conditions were close to the values measured in the reference vessel and not exceedingly high like the values before stent placement.
Implications for WIA

It is important to note that our critique of the single-point technique concerns mainly the case of a diseased coronary vessel. We confirmed that the separated WI remains relatively unchanged for large variations of the wave speed in normal vessels [3, 6] and that this conclusion also applies in diseased vessels and after revascularization. This suggests that even if the single-point technique yields values that considerably over- or underestimate the true wave speed, it can still provide a useful parameter for wave separation. This is an important finding since it enables the separation of traveling waves in the coronary arteries into forward and backward components and therefore allows for a better understanding of aortic, left ventricular and microcirculatory interactions in the coronary circulation.

Conclusions

We conclude that coronary wave speed derived from the single-point technique is coupled to changes in microvascular resistance, MR, which limits its applicability to study local wall properties or physiological responses. Despite the fact that c may not accurately represent true wave speed in diseased coronary arteries, it still is a useful parameter for the purpose of wave separation in coronary WIA applications.

References


[16] Reneman RS, Meinders JM and Hoeks APG, Non-invasive ultrasound in arterial wall dynamics in humans: What have we learned and what remains to be solved. Eur Heart J 26:960-966, 2005


