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Use of a Pressure Wire for Automatically Correcting Artifacts in Phasic Pressure Tracings From a Fluid-Filled Catheter

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ABSTRACT

Background/purpose: Matching phasic pressure tracings between a fluid-filled catheter and high-fidelity pressure wire has received limited attention, although each part contributes half of the information to clinical decisions. We aimed to study the impact of a novel and automated method for improving the phasic calibration of a fluid-filled catheter by accounting for its oscillatory behavior.
Methods/materials: Retrospective analysis of drift check tracings was performed using our algorithm that corrects for mean difference (offset), temporal delays (timing), differential sensitivity of the manifold transducer and pressure wire sensor (gain), and the oscillatory behavior of the fluid-filled catheter described by its resonant frequency and damping factor (how quickly oscillations disappear after a change in pressure).
Results: Among 2886 cases, correcting for oscillations showed a large improvement in 28 % and a medium improvement in 41 % (decrease in root mean square error >0.5 mmHg to <1 or 1-2 mmHg, respectively). 96 % of oscillators were underdamped with median damping factor 0.27 and frequency 10.6 Hz. Fractional flow reserve or baseline Pd/Pa demonstrated no clinically important bias when ignoring oscillations. However, uncorrected subcycle non-hyperemic pressure ratios (NHPR) displayed both bias and scatter.
Conclusions: By automatically accounting for the oscillatory behavior of a fluid-filled catheter system, phasic matching against a high-fidelity pressure wire can be improved compared to standard equalization methods. The majority of tracings contain artifacts, mainly due to underdamped oscillations, and neglecting them leads to biased estimates of equalization parameters. No clinically important bias exists for whole-cycle metrics, in contrast to significant effects on subcycle NHPR.

1. Introduction

Invasive pressure measurements in the cardiovascular system form the basis for both patient monitoring and clinical diagnosis. These assessments almost always use fluid-filled catheters for a variety of reasons, chiefly cost and ease of insertion. However, high-fidelity, in situ pressure sensors, either piezoelectric or fiberoptic, have found growing application for coronary and valvular stenosis using metrics like fractional flow reserve (FFR), non-hyperemic pressure ratios (NHPR), mean transvalvular pressure gradient (ΔP), and the stress aortic valve index (SAVI) [1].

Regardless of the specific application, the pressure wire must be matched with the fluid-filled catheter, a process termed “equalization” or “normalization” depending on the platform. Typically this agreement focuses only on mean pressure since FFR (the most common clinical metric) averages the entire cardiac cycle. However, NHPR and aortic valve assessments depend on just part of the cardiac cycle, generally diastole or systole, respectively. Matching phasic pressure tracings between a fluid-filled catheter and a high-fidelity pressure wire has received limited

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attention, although each part contributes half of the information used for a clinical decision.

Recently we introduced a novel and automated method for improving the phasic calibration of a fluid-filled catheter by accounting for its oscillatory behavior [2]. However, that "proof of concept" needed to be applied to a large number of pressure tracings in order to address several practical points. First, how much improvement in equalization can be expected by accounting for oscillations? Second, what proportion of fluid-filled pressure tracings contains significant oscillation? Third, how and when does correcting these artifacts on the catheter signal impact whole-cycle metrics like FFR versus sub-cycle metrics like NHPR? Finally, which physical properties of the catheter, tubing, and manifold account for the oscillatory behavior? To answer these questions, we pooled a large number of tracings with the goal of improving clinical pressure measurements via automated software algorithms independent of advances in pressure wire hardware.

2. Materials and methods

2.1. Automated algorithm

Our method for automatically correcting oscillator artifacts on the pressure signal from a fluid-filled catheter has been published previously [2], hereby summarized briefly and further detailed in the supplement. Currently the algorithm is not available commercially. Traditionally the pressure difference between the catheter and pressure wire has been attributed solely to hydrostatic offset between the two systems, originally adjusted by changing the height of the manifold transducer until its mean pressure matched that of the pressure wire [3], now performed internally by software. While sufficient for average pressure readings, this rudimentary equalization neglects phasic distortions introduced by a fluid-filled system, classically described for 60 years as behaving like a damped harmonic oscillator (mass on a spring with friction) [4].

Depending on the pressure wire platform, existing clinical software accounts for three mechanisms to match phasic pressures [2]. First, the term "offset" refers to the mean pressure difference between the fluid-filled catheter and pressure wire sensor. Second, the term "timing" refers to temporal delays between the arrival of the pressure signals from the two devices, attributed to catheter pressure propagation delay and heterogeneous electronic processing. Third, the term "gain" refers to a differential response of the manifold transducer and pressure wire sensor to the same change in absolute pressure (for example, a pressure increase of 10 mmHg for one sensor might produce an increase of 11 mmHg for the other sensor, equivalent to a unitless gain factor of $11/10 = 1.1$ or $10/11 = 0.91$ depending on the definition).

In addition to these three mechanisms, our novel algorithm automatically also accounts for the oscillatory behavior of the fluid-filled catheter observed clinically and described by its resonant frequency (driving the system at this natural period will result in increased oscillations) and a damping factor (how quickly oscillations disappear after a change in pressure, usually denoted by the Greek letter zeta ζ). Damping factors <1 indicate an underdamped system ("ringing"), factors >1 indicate an overdamped system (no ringing, but a slow return to the true pressure), and a value of 1 indicates critical damping (fastest return to the true pressure without oscillation). As visually summarized in Fig. 1, the algorithm optimizes the root mean square (RMS) difference between the phasic catheter and pressure wire signals during equalization to determine the best offset, timing difference, gain, and oscillator frequency and damping factor (total of 5 parameters).

Note that we believe that the pressure wire provides the superior reference between the two signals given its per-wire customized pressure calibration and greater fidelity. While clearly true for phasic pressures, we also maintain that this superiority holds for absolute pressures and therefore the pressure offset, given its more extensive and customized calibration at the time of manufacture. The offset can be trivially reversed for users or situations that prefer to keep the same mean arterial pressure as the manifold.

2.2. Pressure tracings

We compiled digital pressure tracings from 6 previously published studies of coronary physiology [5–10]. In brief, each study enrolled typical patients undergoing routine invasive cardiac catheterization with FFR assessment as per standard practice, generally as part of trials to determine diagnostic accuracy. Pressure wires were from either St Jude/Abbott [5–7,9] or Volcano/Philips [10] and tracings came from subjects in 16 countries over 4 continents: Australia [7], Belgium [6,9], Czech Republic [9], Denmark [7], England [7], France [6], Germany [7], Italy [6], Japan [7],

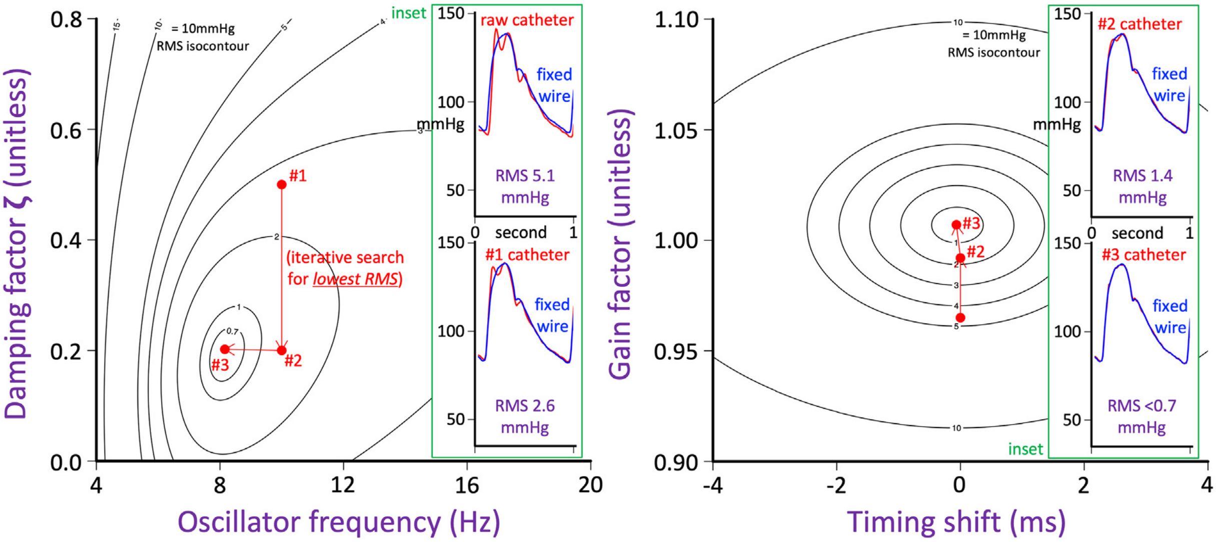

Fig. 1. Conceptual and visual description of the fitting algorithm. The algorithm seeks 5 parameters to minimize the root mean square (RMS) error between the pressure wire (blue, reference standard) and the fluid-filled catheter (red) phasic pressure tracings shown in the green insets for an example case. Its 5 parameters are the harmonic oscillator frequency and damping factor (displayed on the left map with RMS isocontours), timing shift and gain factor (displayed on the right isocontour map), and mean hydrostatic pressure offset (not shown). Starting at red point #1 (with an arbitrary 10 Hz frequency and 0.5 underdamped oscillator), the optimal values for the other 3 parameters are found. With each iteration the algorithm decreases the RMS error using non-linear optimization. For example, the algorithm eventually moved to point #2 that reduced the RMS to 1.4 mmHg before finding the best fit at point #3 with an RMS <0.7 mmHg.

Latvia [7], Netherlands [6,9], Portugal [6], Scotland [6–10], South Korea [5–7], Sweden [9] [6], and the United States [6]. We sought no additional institutional board review for this retrospective analysis because each subject had already provided written informed consent as part of the initial study and the anonymous pressure tracings contained no confidential identifiers.

Manual, central review of tracings (DTJ, NPJ) identified a subset with a final drift check, when the pressure wire was returned for at least 3 recorded beats to the tip of the guide catheter after distal assessment. Gross overdamping or ventricularization of the aortic pressure tracing, whip on the pressure wire tracing, and marked arrhythmia were also reasons for exclusion. Only one tracing per vessel was permitted, but multiple, independent vessels per subject were accepted as long as each vessel had its own drift check.

Each drift check was automatically corrected by our algorithm in stepwise fashion for a total of 5 separate models: raw tracing (no corrections), offset only (1 parameter), offset plus timing (2 parameters), offset and timing plus gain (3 parameters), and offset and timing and gain plus oscillator frequency and damping factor (5 parameters). For each equalization model, the associated baseline and peak hyperemic portions of the tracing (if present and valid) were adjusted accordingly to permit computation of the baseline coronary-to-aortic pressure ratio over the entire cardiac cycle (so-called resting Pd/Pa) as well as FFR during stable hyperemia. Baseline Pd/Pa tracings were automatically analyzed for a variety of NHPR using the CoroFlow software package from Coroventis [11]: dPR (diastolic pressure ratio [12]), iFR (instantaneous wave-free ratio [13]), and RFR (resting full-cycle ratio [14]). Additionally, DFR (diastolic hyperemia-free ratio) was computed using its published description [15]. Finally, we compared a model using offset only (1 parameter) against 3 models adding a second parameter (timing, gain, or oscillator) to determine their relative importance.

2.3. Statistical methods

Analyses were performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). We employed standard statistical techniques. Applicable tests were two-tailed, and $p < 0.05$ was considered statistically significant. Variances were compared using the Brown-Forsythe test with no adjustment for multiple testing. Anonymous pressure tracings for each vessel, including baseline, hyperemia, and drift check, have been made publicly available [16].

3. Results

3.1. Improvement in phasic equalization

From the 6 previously published studies [5–10], we included 2886 of 3803 (75.9 %) potential vessels after applying the inclusion and exclusion criteria. The median number of valid beats for the drift check was 6 (interquartile range [IQR] 4 to 11). Fig. 2 (left) depicts the phasic agreement between the pressure wire and fluid-filled catheter during the drift check among 5 sequential equalization models, quantified by the root mean square (RMS) difference in mmHg. A linear, mixed effects, repeated measures ANOVA (to account for multiple equalization models per drift check) demonstrated a significant $p < 0.001$ difference among models, and the Tukey all-pair comparison showed significantly $p < 0.001$ lower RMS between each stepwise pair.

Fig. 2 (right) demonstrates the improvement in phasic matching when adding an oscillator, even after accounting for drift, timing, and gain. Only 24 % of drift checks showed minimal improvement (change Δ in RMS ≤ 0.5 mmHg), with just 15 tracings (0.5 %) becoming worse (larger RMS). Conversely, 28 % of cases showed a large improvement (Δ > 0.5 mmHg to a final RMS < 1 mmHg), 41 % showed a medium improvement (Δ > 0.5 mmHg to a final RMS = 1-2 mmHg), and a small 7 % were better but with a poor residual fit (Δ > 0.5 mmHg but final RMS > 2 mmHg).

3.2. Physical properties of fluid-filled catheter systems

Fig. 3 provides histograms of the damping factor and frequency in the 1991 drift checks with an important oscillator (Δ > 0.5 mmHg to a final RMS ≤ 2 mmHg). A 96 % majority of oscillators behaved in an

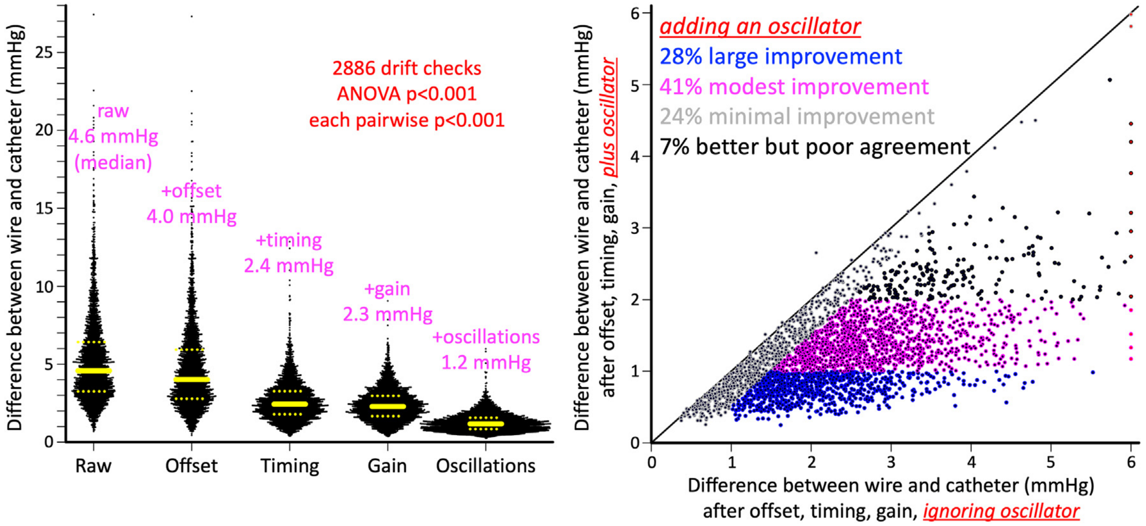

Fig. 2. (left) Sequential improvement in phasic matching of fluid-filled catheter and pressure wire. For all drift checks, the phasic agreement between the fluid-filled guide catheter and the 0.014″ high-fidelity pressure wire was quantified using the root mean square (RMS) difference. Five different equalization models were studied: raw (no corrections), offset (removing mean pressure difference between the tracings), timing (offset plus shifting the curves backwards/forwards in time), gain (offset and timing plus permitting differential gain response between the two pressure signals), and oscillator (offset and timing and gain plus accounting for the harmonic oscillator behavior of a fluid-filled catheter system). Repeated measures ANOVA detected a systematic difference ($p < 0.001$) among models, with each pair demonstrating a significant reduction in the RMS value ($p < 0.001$) via Tukey paired comparisons. Yellow bars indicate the median and interquartile range of each distribution, with the median value explicitly given in magenta text. (right) Importance of including an oscillator. For all drift checks, accounting for the oscillatory behavior of the fluid-filled catheter almost always improved the root mean square (RMS) difference compared to a 0.014″ high-fidelity pressure wire. While only the 24 % of points (grey) showed minimal improvement (change Δ in RMS ≤ 0.5 mmHg), 28 % (blue) showed a large improvement (Δ > 0.5 mmHg to a final RMS < 1 mmHg), 41 % (magenta) showed a modest improvement (Δ > 0.5 mmHg to a final RMS = 1-2 mmHg), and a small 7 % (black) were better but with a poor residual fit (Δ > 0.5 mmHg but final RMS > 2 mmHg). Note that 13 cases with RMS > 6 mmHg when ignoring the oscillator have been displayed at this upper bound; no case had an RMS > 6 mmHg after accounting for the oscillator.

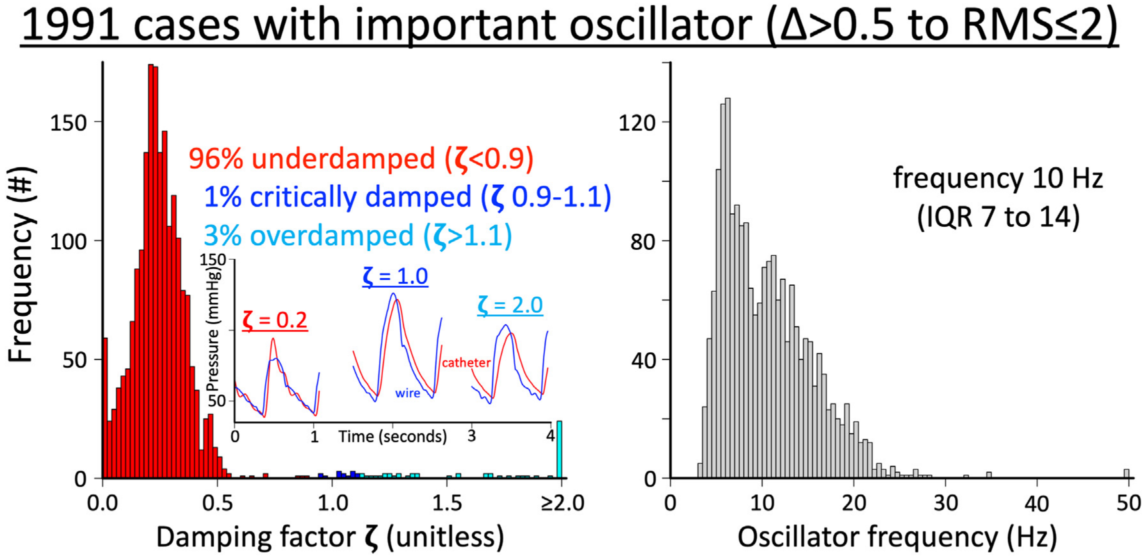

Fig. 3. Histograms of important oscillator parameters. The vast majority 96 % (red) of important oscillators behave in an underdamped ("ringing", damping factor < 0.9) fashion, while only 1 % (blue) are nearly critically damped (damping factor 0.9–1.1) and just 3 % (cyan) overdamped (damping factor > 1.1). The frequency distribution of oscillators skews to the right with a median value of 10 Hz. The inset shows 1-beat examples of phasic pressure tracings from the wire (blue) and catheter (red) for underdamped, critically damped, and overdamped cases. Note the upper limit on the right of 50 Hz equal to the maximum value allowed by our algorithm given typical 25 Hz roll-off in pressure wire response.

underdamped fashion ("ringing", factor < 0.9), with just over 95 % of damping factors <0.5, summarized by median values of 0.24 (subset of drift checks with important oscillators) to 0.27 (all drift checks) in Table 1. Only 1 % of important oscillators were nearly critically damped (factor from 0.9 to 1.1) and 3 % overdamped (factor > 1.1).

Oscillator frequency in Fig. 3 skewed rightward toward higher values (as one might expect for a logarithmic spectrum) with median of 9.7 Hz (IQR 6.5 to 13.6). The lowest and highest frequencies equaled 3.2 and 50 Hz, respectively, with 50 Hz equal to the maximum value allowed by our algorithm given typical 25 Hz roll-off in pressure wire response (upper bound for frequency determined by the sampling rate and low-pass filter).

Table 1 summarizes the equalization model parameters for the entire cohort as well as the subset with an important oscillator ($\Delta >$ 0.5 mmHg to a final RMS ≤ 2 mmHg). Notably, biased estimates of the timing difference arose when ignoring the oscillator. Fig. 4 (left) details how the "apparent timing difference" of +14 ms (IQR +6 to +26) almost disappeared when taking the oscillator into account (median + 1.8 ms, IQR −1.9 to +4.5). After removing important oscillator artifacts, 66.5 % of such tracings had a timing difference within ±5 ms of zero, that is within 1 sample during standard 100 Hz recording. Paired *t*-tests demonstrated that adding an oscillator reduced the apparent timing difference significantly ($p < 0.001$ versus either timing alone or timing plus gain).

Accounting for gain increased the offset (paired *t*-test $p < 0.001$ versus offset and shift) and decreased the gain (paired t-test $p < 0.001$ versus adding the oscillator), highlighting the ambiguous and artifactual tradeoff between these two parameters when ignoring oscillations; expectedly, accounting for gain did not change the apparent timing difference ($p = 0.287$). Although average differential gain when accounting for the oscillator was approximately 1 with negligible timing difference, their distributions in the population differed significantly from these fixed values ($p < 0.001$) assumed by a standard equalization that accounts only for hydrostatic pressure offset [3]. Finally, starting with an offset correction and separately adding one additional parameter demonstrated differential effects on decreasing RMS ($p < 0.001$ by repeated measures ANOVA): gain −0.2 mmHg (IQR −0.3 to −0.1); timing −1.1 mmHg (IQR −2.5 to −0.5); and oscillations −2.6 mmHg (IQR −4.1 to −1.5). Each difference in RMS was significant $p < 0.001$ by a Tukey all-pair comparison, indicating that removing oscillation artifacts provides the single largest improvement in phasic matching after accounting for hydrostatic offset.

Table 1

Impact of equalization method on matching parameters. The formatting of this table in the PDF proof is very poor. It needs to be wider, probably two columns in width, in order for the cell entries to be on a single line or maybe two lines. Currently many cells are three lines tall, which is basically impossible to read clearly.

Equalization	Offset (mmHg)	Timing shift (ms)	Gain (unitless)	Damping (unitless)	Frequency (Hz)	RMS (mmHg)
All tracings (n = 2886)						
Offset only	−1.1 (−2.1 to −0.1)	0	1	NA	NA	4.0 (2.8 to 5.9)
Plus timing shift	−1.1 (−2.2 to −0.1)	14.4 (6.2 to 26.7)	1	NA	NA	2.4 (1.8 to 3.3)
Plus gain	+1.6 (−1.1 to +4.4)	14.3 (6.1 to 26.7)	0.969 (0.937 to 0.996)	NA	NA	2.3 (1.7 to 3.0)
Plus oscillator	−1.9 (−4.0 to −0.0)	2.1 (−2.2 to 5.2)	1.008 (0.993 to 1.029)	0.27 (0.19 to 0.40)	10.6 (6.9 to 15.0)	1.2 (0.8 to 1.6)
Important[a] oscillator (n = 1991)						
Offset only	−1.1 (−2.0 to −0.1)	0	1	NA	NA	4.0 (2.9 to 5.8)
Plus timing shift	−1.1 (−2.0 to −0.2)	13.9 (6.2 to 25.5)	1	NA	NA	2.6 (2.1 to 3.3)
Plus gain	+2.5 (+0.1 to +5.1)	13.9 (6.2 to 25.5)	0.958 (0.928 to 0.982)	NA	NA	2.4 (1.9 to 3.0)
Plus oscillator	−1.7 (−3.7 to +0.1)	1.8 (−1.9 to 4.5)	1.006 (0.992 to 1.028)	0.24 (0.18 to 0.32)	9.7 (6.5 to 13.6)	1.1 (0.8 to 1.4)

Abbreviations: Hz = Hertz (1/second); mmHg = pressure in millimeters of mercury; ms = millisecond; RMS = root mean square difference between fluid-filled catheter and high-fidelity 0.014″ pressure wire. Summary values represent median (interquartile range, IQR).

[a] Change in root mean square (RMS) difference between pressure wire and fluid-filled catheter during the drift check of >0.5 mmHg to a final RMS ≤ 2 mmHg when adding the oscillator.

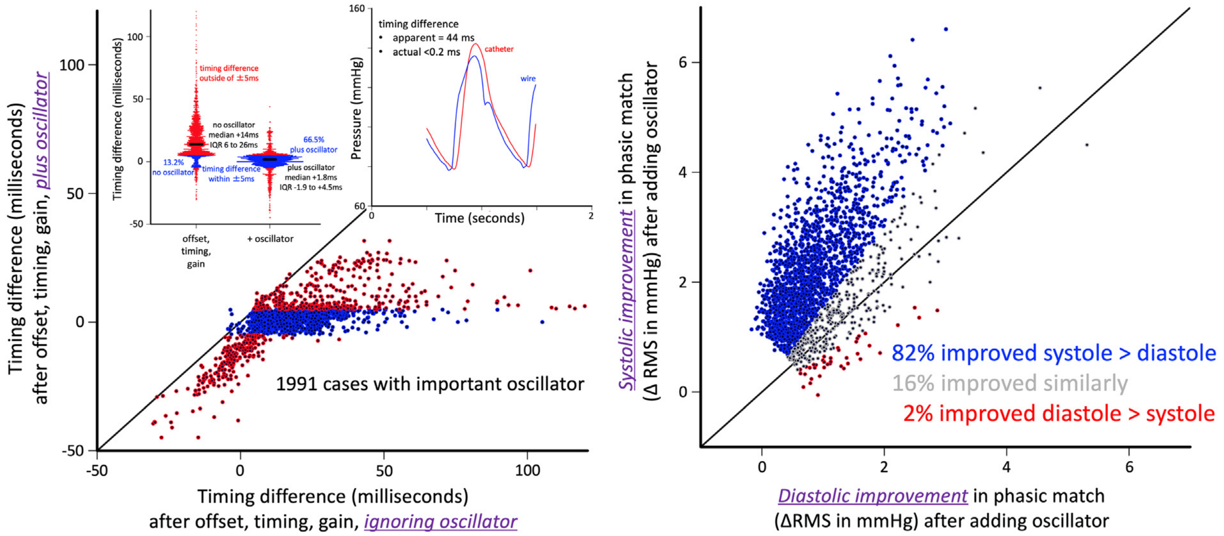

Fig. 4. (left) Biased estimate of timing difference when neglecting an important oscillator. A timing difference between the fluid-filled catheter pressure signal and that from a high-fidelity 0.014″ pressure wire might exist due to a variety of mechanisms like catheter pressure propagation delay and heterogeneous electronic processing. When ignoring the oscillatory behavior, an apparent median timing difference of +14 ms (interquartile range [IQR] +6 to +26) existed, yet almost vanished to +1.8 ms (IQR −1.9 to +4.5) when adjusting for the oscillator artifact. Points in blue denote timing differences within ±5 ms, equivalent to 1 sample during standard 100 Hz recording, much more common (66.5 %) when accounting for the oscillator than when neglecting it (13.2 %). The inset tracing in the upper right shows 1 beat from a case with a large apparent timing difference that completely disappeared after removing the oscillator artifact. (right) Subcycle impact of an important oscillator on phasic matching. The systolic (first third of the cardiac cycle) improvement in root mean square (RMS) difference between the fluid-filled catheter and high-fidelity 0.014″ pressure wire generally exceeded diastolic (final two-thirds of the cardiac cycle) improvement when adding a harmonic oscillator to an equalization that already accounted for offset, timing differences, and gain. A 82 % majority (blue points) demonstrated greater systolic than diastolic improvement (diastolic/systolic RMS improvement >1.5). Only a 2 % minority (red points) improved the diastolic match substantially more than the systolic match (systolic/diastolic RMS improvement >1.5), whereas 16 % (grey points) displayed similar improvement in both parts of the cardiac cycle.

3.3. Clinical impact of removing oscillator artifact

Fig. 4 (right) compares the relative impact of accounting for the oscillator on phasic matching of systole (defined as the first third of the cardiac cycle) versus diastole (the final two-thirds of the cardiac cycle). As quantified by the decrease in subcycle RMS when adding the oscillator, a 82 % majority of tracings demonstrated greater systolic than diastolic improvement (diastolic/systolic RMS improvement >1.5). Only a 2 % minority improved the diastolic match substantially more than the systolic match (systolic/diastolic RMS improvement >1.5), whereas 16 % displayed equal improvement in both parts of the cardiac cycle.

After matching for all 5 parameters, median FFR equaled 0.81 (IQR 0.73 to 0.87), baseline Pd/Pa 0.94 (IQR 0.90 to 0.98), iFR 0.92 (IQR 0.85 to 0.97), dPR 0.92 (IQR 0.86 to 0.97), RFR 0.92 (IQR 0.85 to 0.96), and DFR 0.92 (IQR 0.85 to 0.97) in our cohort. Table 2 quantifies the impact of sequential matching parameters on whole-cycle physiologic metrics FFR and baseline Pd/Pa (available for 2622 vessels) and on subcycle NHPR (available for 2485 vessels) using the full 5-parameter match as the reference. Fig. 5 displays the Bland-Altman plots for all metrics between matching for offset only (the historic default) and matching for all 5 parameters (using our algorithm).

For whole-cycle physiology (either FFR or baseline Pd/Pa), accounting for offset brought the mean difference to ≤0.001, indicating no clinically important bias. For subcycle NHPR, ignoring oscillations produced a bias of approximately 0.01 (systematically lower NHPR values when accounting only for offset than when accounting for all 5 parameters) whereas accounting for both offset and timing eliminated it to <0.01. The scatter introduced by ignoring oscillations (standard deviation of differences from the 5-parameter correction) was <0.005 for whole-cycle metrics after accounting for offset but smaller for FFR than Pd/Pa (Brown-Forsythe *p*-value <0.001). Scatter increased significantly when adjusting whole-cycle metrics for gain but not oscillations (Brown-Forsythe $p < 0.001$). Subcycle NHPR contained more scatter than whole-cycle baseline Pd/Pa even after adjusting for offset and timing (all Brown-Forsythe $p < 0.001$).

Table 2
Impact of equalization on FFR and NHPR using Bland-Altman analysis.

	Raw	Offset only	Plus timing shift	Plus gain	Plus oscillator
FFR	Δ 0.0104	Δ −0.0007	Δ −0.0009	Δ −0.0021	Δ 0
	±0.0169	±0.0039	±0.0039	±0.0074	(reference)
rest Pd/Pa	Δ 0.0112	Δ −0.0012	Δ −0.0013	Δ −0.0046	
	±0.0188	±0.0048	±0.0048	±0.0114	
iFR	Δ 0.0216	Δ 0.0076	Δ −0.0032	Δ −0.0010	
	±0.0269	±0.0167	±0.0125	±0.0144	
dPR	Δ 0.0192	Δ 0.0055	Δ −0.0049	Δ −0.0037	
	±0.0258	±0.0157	±0.0123	±0.0146	
RFR	Δ 0.0248	Δ 0.0124	Δ −0.0029	Δ −0.0025	
	±0.0269	±0.0186	±0.0094	±0.0118	
DFR	Δ 0.0182	Δ 0.0041	Δ −0.0048	Δ −0.0025	
	±0.0257	±0.0139	±0.0095	±0.0111	

Abbreviations: DFR = diastolic hyperemia-free ratio; dPR = diastolic pressure ratio; FFR = fractional flow reserve; iFR = instantaneous wave-free ratio; NHPR = non-hyperemic pressure ratio; RFR = resting full-cycle ratio. Summary values represent Bland-Altman Δ = mean of difference (when accounting for offset, timing shift, gain, and oscillations) and ± = standard deviation of differences.

4. Discussion

Approximately 2 of every 3 pressure tracings using a fluid-filled catheter in the cardiac catheterization laboratory is significantly distorted by oscillations. These artifacts can be automatically identified and removed by our software algorithm, thereby significantly improving the phasic match with a high-fidelity 0.014″ pressure wire. Neglecting the oscillatory behavior of the fluid-filled pressure signal leads to biased corrections for timing differences and gain factors. Underdamped (“ringing”) oscillators account for the vast majority. Phasic matching improves most during systole, although both parts of the cardiac cycle often improve in parallel. Whole-cycle metrics FFR and baseline Pd/Pa remain insensitive to oscillation artifacts, with very few cases changing by >0.01 in either direction. However, ignoring

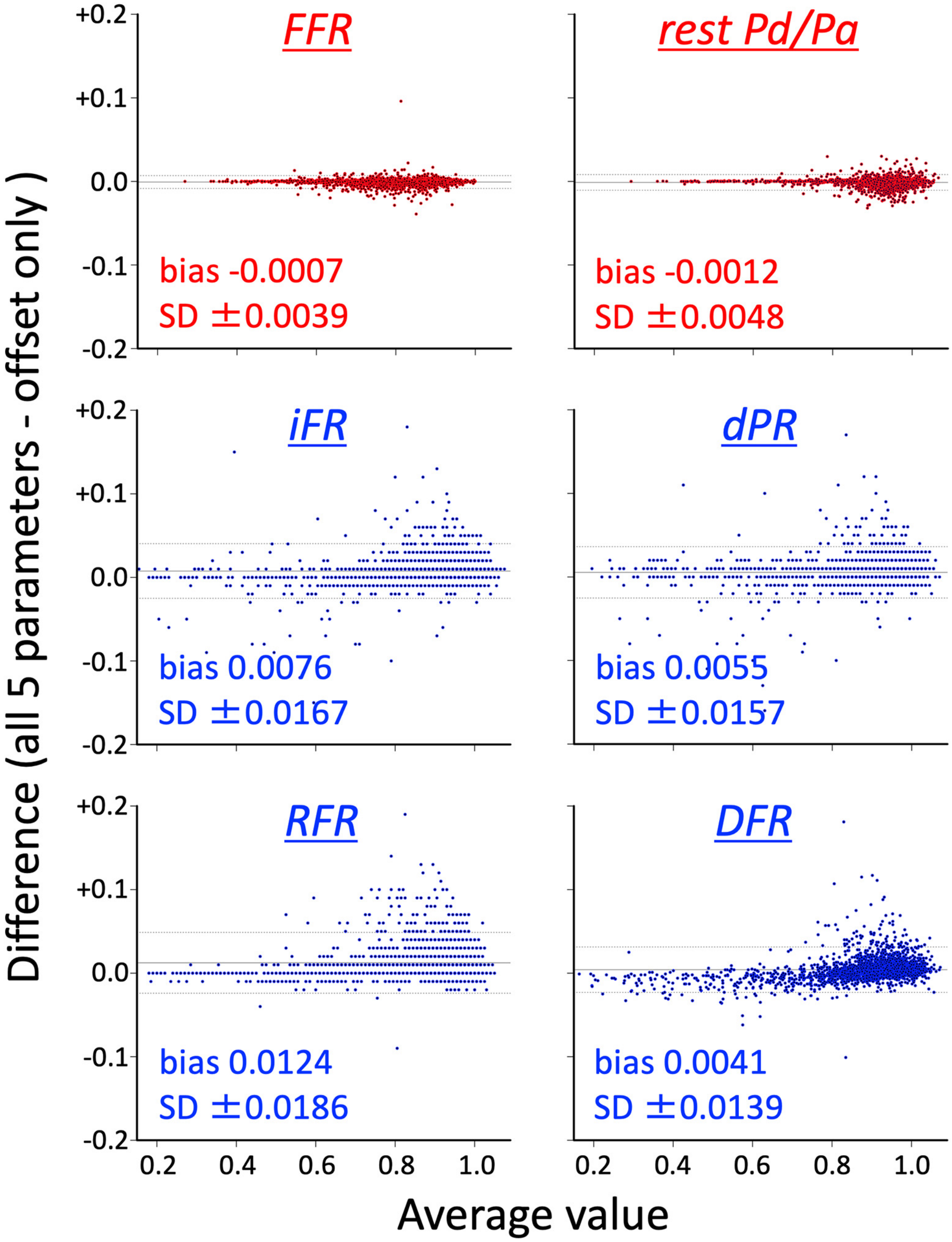

Fig. 5. Impact of oscillations on coronary physiology metrics. For all drift checks, whole-cycle baseline Pd/Pa or fractional flow reserve (FFR, shown in red) demonstrated no clinically important bias as quantified by these Bland-Altman plots of matching offset only (the historic reference standard) versus matching for all 5 parameters (our algorithm). However, subcycle non-hyperemic pressure ratios (NHPR, shown in blue) displayed larger scatter and greater bias when ignoring oscillations. These plots visually present the quantitative results summarized in the "offset only" column of Table 2; horizontal lines plot the mean difference and its 95 % confidence interval (so-called bias and limits of agreement). Note that three of the NHPR metrics had a precision of 0.01 leading to overlap of points. SD = standard deviation.

oscillations significantly affects subcycle NHPR, although adjusting with timing differences can partially compensate.

As demonstrated by Fig. 2 and Table 1, the net improvement in phasic equalization by accounting for hydrostatic offset, timing differences, differential gain, and oscillatory behavior can reach a median root mean square (RMS) difference of 1.2 mmHg. This excellent agreement supports our prior findings that most fluid-filled catheters can be corrected to a 1 mmHg RMS match against a high-fidelity 0.014″ pressure wire [2]. Additionally, our automatic software algorithm removes outliers with poor phasic matching, as seen by the "tighter" distribution in Fig. 2 after accounting for oscillation. Since 28 % of cases demonstrate a large improvement in RMS matching, and 41 % a medium improvement – together 69 % considered important improvements – oscillation significantly affects the majority of tracings.

The larger impact of oscillation on systolic matching reflects the greater dynamic range and higher frequency content of this portion of the cardiac cycle compared to the smaller and more gradual pressure decline during diastole. Consequently, aortic stenosis metrics like the mean transvalvular pressure gradient (ΔP) – usually measured using two fluid-filled systems – and stress aortic valve index (SAVI) [1] experience the greatest distortion from the oscillatory behavior of fluid-filled pressure measuring systems, as discussed previously [2]. Because whole-cycle coronary physiology metrics like FFR and baseline Pd/Pa do not depend on the phasic shape of the pressure tracings, but only on their average values, their insensitivity to improved phasic matching is not surprising. However, subcycle NHPR metrics not only display more sensitivity to oscillations (as reflected by larger bias and limits of agreement in Table 2 compared to whole-cycle metrics) but require at least a correction for timing in order to reduce bias to clinically insignificant levels.

That most oscillators behave in an underdamped fashion reflects the clinical practicalities of pressure measuring systems. Nevertheless, our algorithm can identify and correct all types of oscillators, as seen in Fig. 3, with potential application to automatic contrast injector systems that tend to over-dampen the phasic aortic pressure tracing. The median frequency around 10 Hz in Fig. 3 falls not only below the typical 25 Hz roll-off in pressure wire response but also within the first several harmonics of a typical heart rate during vasodilator stress (120 beats/min equals 2 Hz), indicating its clinical relevance.

Notably, adding an oscillator correction provided the largest improvement in RMS agreement between the fluid-filled catheter and high-fidelity 0.014″ pressure wire after accounting for hydrostatic offset. Therefore, oscillation artifacts represent the single best opportunity to improve phasic agreement especially since, as quantified in Table 1 and Fig. 4, the apparent timing difference between catheter and wire essentially disappears after removing oscillation artifacts. Consequently, implementing a timing difference without accounting for oscillations (as currently done by two commercial vendors of pressure wires) can be considered to be a crude “half oscillator” correction since oscillations introduce delay. Furthermore, our results also suggest two ways to remove oscillation artifacts from a fluid-filled catheter without an independent pressure wire as reference: use fixed values (for example, 11 Hz frequency and 0.27 damping factor derived from Table 1) or match against an idealized aortic waveform shape (for example, derived from the large cohort of tracings in this study).

Classically a fluid-filled catheter has been described as a damped harmonic oscillator (mass on a spring with friction) [4]. As further detailed in the supplement, including theoretical background and benchtop experimental data, we note that a harmonic oscillator only approximates the complete description of a transmission line [4] encompassing all the elements along the chain in the cardiac catheterization laboratory, from guide catheter to stopcocks to pressure tubing to the manifold transducer. While Fig. 2 demonstrates that vast improvements can be made using a harmonic oscillator simplification, our work emphasizes the incomplete nature of this description and potential future avenues for refinement. Furthermore, our results in the supplement explain the observed stability of the oscillation parameters during routine coronary and valvular assessments [2], since they predominately arise from physical properties of the transmission line components and not from transient air bubbles in the fluid-filled system.

4.1. Comparison to existing literature

To our knowledge and excepting our previous publication [2], no prior work has proposed using a high-fidelity 0.014″ pressure wire to improve the phasic matching of the fluid-filled catheter pressure using a harmonic oscillator model in automated fashion. However, an extensive literature over the past 60 years [4] has explored other methods for evaluating the frequency response of fluid-filled catheter systems. We believe that using manometer-tipped devices and an impulse-response technique (so-called “pop” or “snap” tests) does not offer a practical solution. Our software algorithm can be automatically applied in a short period of time (median 6 beats in this study), no different than current “equalization” or “normalization” as in routine practice.

4.2. Limitations

Due to the design of the underlying studies, we applied our analysis to drift checks recorded after coronary assessment, not during the initial equalization period. Therefore the difference in Fig. 2 between the raw tracing (median 4.6 mmHg) and application of offset (median 4.0 mmHg) largely reflects pressure drift during the distal coronary measurements and minimizes initial hydrostatic differences between the manifold transducer and pressure wire that have already been accounted for by equalization. Therefore, we cannot directly compare the relative impact of hydrostatic and oscillator effects on RMS differences. Additionally, based on our prior work that showed stability of other parameters during typical intracoronary instrumentation [2], we do not believe that an important bias arose due to our analysis of drift checks instead of equalization recordings. The current cohort was not enrolled prospectively for the explicit purpose of studying our hypothesis, but rather served as a retrospective cohort of convenience, with all the associated caveats. Nevertheless, we believe that the large number of tracings from diverse sources (2886 vessels from 6 studies, recorded in 16 countries over 4 continents) sufficiently reflects real-world practice.

5. Conclusions

By automatically accounting for the oscillatory behavior of a fluid-filled catheter system, phasic matching against a high-fidelity 0.014″ pressure wire can be improved compared to standard equalization methods. In effect, operators could have “pressure wire quality” from a fluid-filled catheter – with no extra clinical effort. The majority of tracings contain artifacts, mainly due to underdamped oscillations, and neglecting them leads to biased estimates of equalization parameters. The improvement in phasic matching predominantly affects systole, with no clinically important bias for whole-cycle metrics like FFR or baseline Pd/Pa but significant effects on subcycle NHPR.

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- DTJ, RLK, KLG, and NPJ received internal funding from the Weatherhead PET Center for Preventing and Reversing Atherosclerosis, and have a patent pending on diagnostic methods for quantifying aortic stenosis and TAVI physiology.
- DTJ, BDB, RLK, KLG, and NPJ have a patent pending on methods used in this manuscript to correct pressure tracings from fluid-filled catheters.
- DTJ reports no additional support or industry relationships.
- JS is the Chief Executive Officer of the private company Coroventis.
- JMA reports no applicable support or industry relationships.
- HGB has a consulting relationship with Abbott Vascular.
- DC reports speaker and consulting fees from Abbott.
- MvtV reports no applicable support or industry relationships.
- BH reports no applicable support or industry relationships.
- BDB has a consulting relationship with Boston Scientific, Abbott Vascular, CathWorks, Siemens, and Coroventis Research; receives research grants from Abbott Vascular, Coroventis Research, Cathworks, Boston Scientific; and holds minor equities in Philips-Volcano, Siemens, GE Healthcare, Edwards Life Sciences, HeartFlow, Opsens, and Celiad.
- RLK reports no additional support or industry relationships.
- KLG is the 510(k) applicant for CFR Quant (K113754) and HeartSee (K143664, K171303, and K202679), software packages for cardiac positron emission tomography image processing, analysis, and absolute flow quantification.
- NPJ has received significant institutional research support from St. Jude Medical (CONTRAST, NCT02184117) and Philips/Volcano Corporation (DEFINE-FLOW, NCT02328820) for other studies using intracoronary pressure and flow sensors; and has an institutional licensing agreement with Boston Scientific for the smart minimum FFR algorithm commercialized under 510(k) K191008. There is no funding source for this manuscript. These are all relationships with industry.

CRediT authorship contribution statement

Daniel T. Johnson: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Visualization. **Johan Svanerud:** Formal analysis,

Investigation, Resources, Data curation, Writing – review & editing. **Jung-Min Ahn:** Investigation, Resources, Data curation, Writing – review & editing, Funding acquisition. **Hiram G. Bezerra:** Investigation, Resources, Data curation, Writing – review & editing, Funding acquisition. **Damien Collison:** Investigation, Resources, Data curation, Writing – review & editing, Funding acquisition. **Marcel van 't Veer:** Formal analysis, Investigation, Resources, Data curation, Writing – review & editing. **Barry Hennigan:** Investigation, Resources, Data curation, Writing – review & editing, Funding acquisition. **Bernard De Bruyne:** Conceptualization, Methodology, Investigation, Resources, Writing – review & editing, Supervision. **Richard L. Kirkeeide:** Conceptualization, Methodology, Validation, Formal analysis, Writing – review & editing, Visualization. **K. Lance Gould:** Conceptualization, Methodology, Writing – review & editing, Visualization, Supervision, Funding acquisition. **Nils P. Johnson:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Visualization, Project administration, Funding acquisition.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2022.07.021.

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