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Phasic pressure measurements for coronary and valvular interventions using fluid-filled catheters: Errors, automated correction, and clinical implications

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Abstract

Objectives: We sought to develop an automatic method for correcting common errors in phasic pressure tracings for physiology-guided interventions on coronary and valvular stenosis.

Background: Effective coronary and valvular interventions rely on accurate hemodynamic assessment. Phasic (subcycle) indexes remain intrinsic to valvular stenosis and are emerging for coronary stenosis. Errors, corrections, and clinical implications of fluid-filled catheter phasic pressure assessments have not been assessed in the current era of ubiquitous, high-fidelity pressure wire sensors.

Methods: We recruited patients undergoing invasive coronary physiology assessment. Phasic aortic pressure signals were recorded simultaneously using a fluid-filled guide catheter and 0.014″ pressure wire before and after standard calibration as well as after pullback. We included additional subjects undergoing hemodynamic assessment before and after transcatheter aortic valve implantation. Using the pressure wire as reference standard, we developed an automatic algorithm to match phasic pressures.

Results: Removing pressure offset and temporal shift produced the largest improvements in root mean square (RMS) error between catheter and pressure wire signals. However, further optimization <1 mmHg RMS error was possible by accounting for differential gain and the oscillatory behavior of the fluid-filled guide. The impact of correction was larger for subcycle (like systole or diastole) versus whole-cycle metrics, indicating a key role for valvular stenosis and emerging coronary pressure ratios.

Conclusions: When calibrating phasic aortic pressure signals using a pressure wire, correction requires these parameters: offset, timing, gain, and oscillations (frequency and damping factor). Automatically eliminating common errors may improve some clinical decisions regarding physiology-based intervention.

KEYWORDS
aortic stenosis, fractional flow reserve, pressure hemodynamics

1 | INTRODUCTION

Appropriate patient selection for intervention on coronary or aortic stenosis requires physiologic assessment. Namely, does the severity reach a level that warrants a therapeutic procedure? While noninvasive physiologic imaging for either of these two pathologies can often provide sufficient quantification, many cases undergo or demand invasive pressure assessment. For coronary stenosis, established fractional flow reserve (FFR) has been joined by nonhyperemic pressure ratios (NHPR).[1] For aortic stenosis, the mean transvalvular pressure gradient (ΔP) remains classic, with emerging data for the stress aortic valve index (SAVI).[2]

A variety of invasive tools can measure pressure but offer tradeoffs. On the one hand, any measurement system that crosses a stenosis will create an iatrogenic gradient, both for coronary[3] and valvular[4] lesions. Smaller devices bias the gradient less than larger devices. On the other hand, smaller diameter, fluid-filled systems do not provide high-fidelity phasic waveforms required by certain types of subcycle metrics like NHPR, ΔP, and SAVI. Hence historic 2F microcatheters[5] and 0.015″ fluid-filled wires[6] gave way to modern, high-fidelity 0.014″ piezoelectric or fiberoptic pressure wires for coronary physiology. While most aortic valve assessment uses single- or dual-lumen pigtail catheters, high-fidelity micromanometers have found limited clinical uptake, in contrast to repurposing coronary pressure wires for valvular assessment.[2,7]

Because of the added cost and logistical complexity of introducing two simultaneous pressure wires, the aortic tracing comes from the guiding catheter. Its calibration has received significantly less attention, although it contributes half of the signal used to quantify the stenosis. Due to the widespread availability, robust handling, and excellent fidelity of commercial pressure wires, we examined their use to calibrate the fluid-filled catheter. In doing so, we developed a novel and automatic software technique to correct for errors commonly present in phasic pressure measurements. Clinically, the practical consequences apply more to subcycle (like systole or diastole) measurements of coronary and valvular stenosis like NHPR, ΔP, and SAVI.

2 | MATERIALS AND METHODS

In order to focus the main manuscript on coronary stenosis, we placed parallel methods, results, and discussion regarding valvular stenosis in the supplement.

2.1 | Calibration of fluid-filled catheter

This section provides an overview of our algorithm to correct the pressure signal from a fluid-filled catheter using a high-fidelity 0.014″ pressure wire as the reference. Further technical details can be found in the supplement. We believe that the pressure wire provides the superior reference between the two pressure signals given its per-wire customized pressure calibration and greater fidelity.[8] While clearly true for phasic pressures, we also maintain that this superiority of the pressure wire holds for absolute pressures, and therefore the pressure offset, given its more extensive and customized calibration at the time of manufacture. If, however, users prefer to keep the same mean arterial pressure as the manifold, then the offset can be trivially reversed. Although we use a pressure wire as the reference standard, our algorithm could straightforwardly use a second fluid-filled catheter with different characteristics as an alternative reference.

Figure 1 contrasts the aortic pressure signal measured using two methods. A fluid-filled catheter behaves like a damped harmonic oscillator (mass on a spring with friction) as has been well understood for decades.[9] These oscillations of fluid (blood, saline, contrast), potential bubbles inside the guide catheter, and the properties of the connection tubing produce the "ringing" instead of the "smooth" tracing provided by the pressure wire.

To match the pressure signal from a fluid-filled catheter against the reference 0.014″ pressure wire requires the series of steps

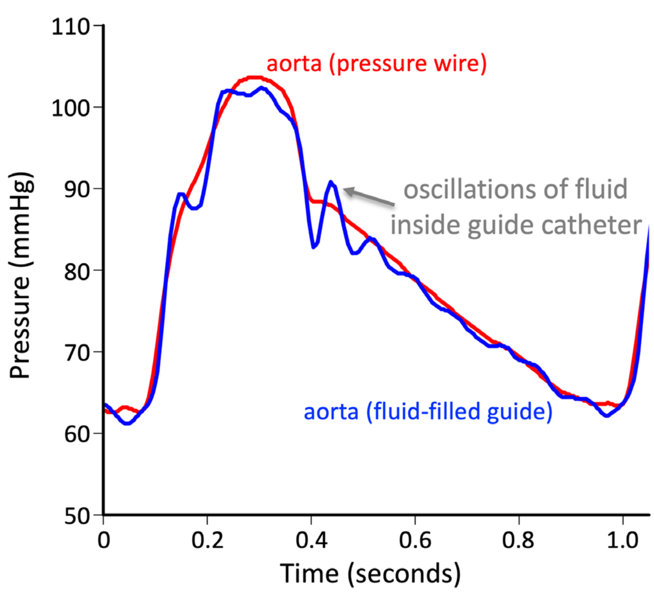

FIGURE 1 Artifacts when measuring pressure using fluid-filled catheters. Aortic pressure from a single cardiac cycle contrasting the signal from a 0.014″ pressure wire (red) with a fluid-filled guide catheter (blue). After matching the tracings for offset, timing, and gain, the fluid-filled guide catheter still displays "ringing" despite vigorous flushing. These oscillations arise from the fluid-filled system's acting like a damped harmonic oscillator, and can be corrected with our described technique [Color figure can be viewed at wileyonlinelibrary.com]

detailed in Figure 2. First, the average reading should agree between the two systems by removing any pressure offset (often related to the height of the fluid-filled manifold transducer[10]). Second, the timing of the two signals might differ due to catheter pressure propagation delay, heterogeneous electronic processing and delays. Third, each sensor has its own signal-to-pressure calibration that might not match, thereby producing differential gain (for example, a pressure increase of 10 mmHg for one sensor might produce an increase of 11 mmHg for the other sensor). Finally, oscillations from the fluid-filled catheter must be removed after quantifying their frequency and damping (how quickly oscillations disappear). These five parameters (offset, timing, gain, harmonic oscillator frequency, and damping) constitute our model for correcting the pressure tracing from the catheter.

We computed the error difference between the corrected catheter and the wire, and used its root mean square (RMS) value as an objective measure to fit our model to the data. Model parameters are derived by a nonlinear optimization of this RMS error, performed for each beat of a baseline recording when the sensors are located together (see the example provided in the supplement). Data from all the baseline beats is reduced by taking the median value of each of the five parameters for the best beats, those whose RMS error falls below its median (the 50% of valid beats with smallest RMS error). Additionally, we explored adding a second harmonic oscillator.

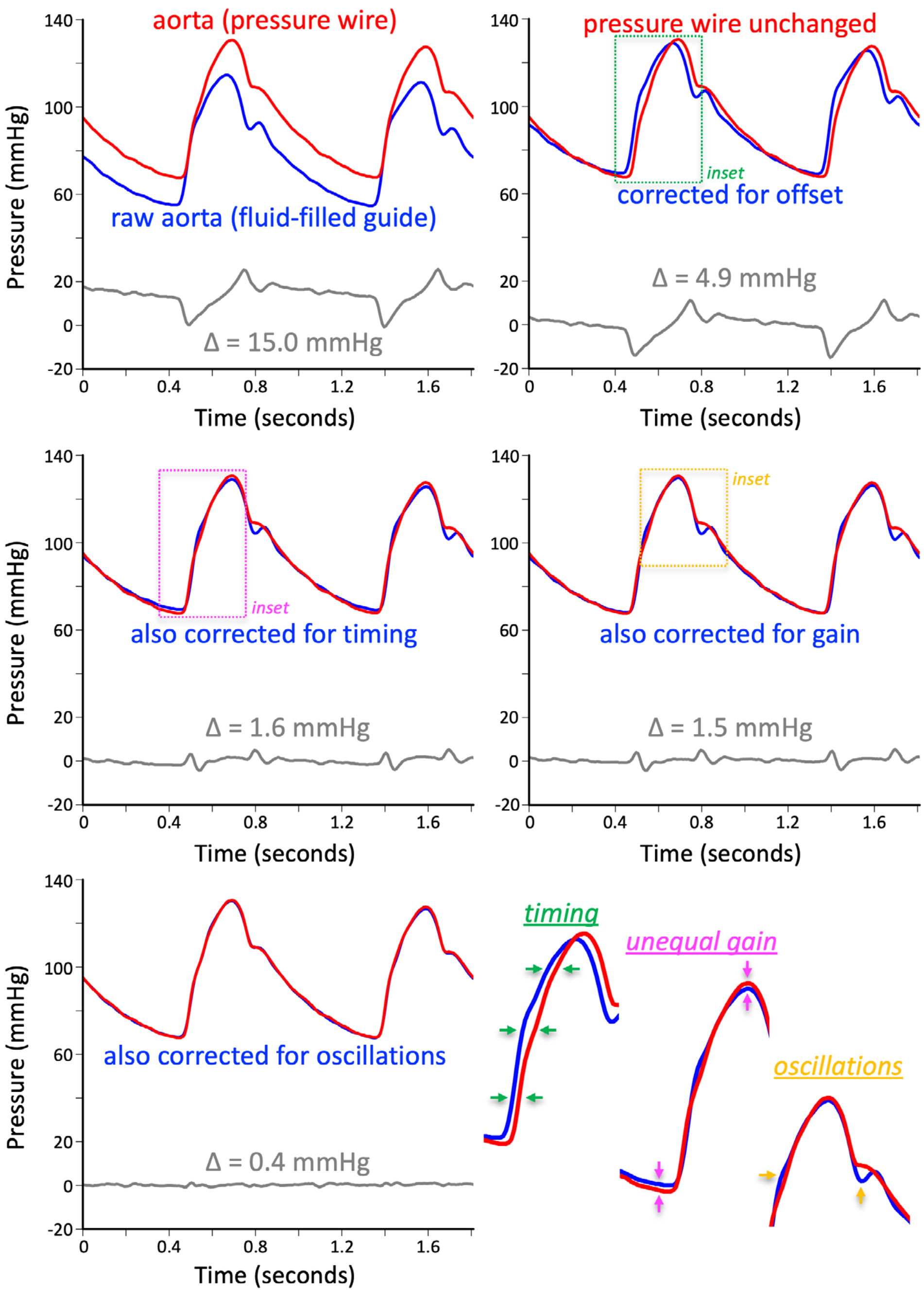

FIGURE 2 Progressive correction of fluid-filled catheter pressure. Matching the raw pressure tracing from a fluid-filled guide catheter (blue) to a high-fidelity 0.014″ pressure wire (red) requires a series of corrections. (Upper left) Raw tracings without any correction. Root mean square (RMS) difference in gray equals about 15 mmHg. (Upper right) After correcting the fluid-filled guide for the average offset, the mean pressures become equal and the RMS difference falls to approximately 5 mmHg. (Middle left) Further correction matches the timing of the two tracings, reducing their RMS difference to 1.6 mmHg. (Middle right) Additionally, the gain can differ between the two pressure transducers, and its correction brings the RMS difference down to 1.5 mmHg in this case. (Lower left) Finally, the oscillatory behavior of the fluid-filled guide catheter can be described using two parameters (frequency and a unitless damping factor), bringing the RMS difference well below 1 mmHg [Color figure can be viewed at wileyonlinelibrary.com]

2.2 | Coronary pressure tracings

From patients undergoing routine FFR assessment for standard indications, we enrolled a convenience cohort at a single center. Subjects gave written informed consent for anonymous use of their pressure tracings and clinical characteristics as part of a general catheterization laboratory protocol approved by the local institutional review board.

As per standard practice, a commercial 0.014″ pressure wire was placed with its sensor at the end of a flushed and disengaged guide catheter after anticoagulation and vasodilator administration. Approximately 30 s of pre-equalization aortic pressure were recorded simultaneously by the pressure wire and guide catheter. Next, the hemodynamic system (Mac-Lab Hemodynamic Recording System, GE Healthcare) performed equalization. Then approximately 30 seconds of post-equalization aortic pressure were recorded. The pressure wire was advanced distally into the vessel of interest and intracoronary adenosine was administered as per routine. Pressure tracings during the onset, peak, and washout of hyperemia were recorded continuously. Finally, the pressure wire was pulled back to the same position as equalization and approximately 30 s of postmeasurement aortic pressure were recorded after appropriate flushing of the guide catheter. Clinical care proceeded as usual with no influence from participation in this study.

Pressure tracings were separated into four parts: pre-equalization, post-equalization, FFR, and pullback drift check. The hemodynamic system exported guide catheter and pressure wire signals to a precision of 0.1 mmHg at a sampling frequency of 240 Hz (approximately 4 ms interval). The three parts of the recording with simultaneous aortic pressures—pre-equalization, post-equalization, and drift check—were analyzed using our 5 parameter model. The hyperemic recording underwent analysis using our previously published algorithm that creates a beat table for each cardiac cycle and calculates the "smart minimum" FFR value.[11] Valid beats underwent further analysis by automatically identifying the diastolic interval on the aortic waveform to compute diastolic FFR.[12]

TABLE 1 Clinical cohort

Number of subjects	23
Age (years)	67.3 ± 8.5
Male (%)	19 (83%)
Body mass index (kg/m^2)	27.3 ± 4.2
Hypertension (%)	13 (57%)
Dyslipidemia (%)	16 (70%)
Diabetes mellitus (%)	8 (35%)
Active or prior tobacco (%)	7 (30%)
Prior myocardial infarction (%)	4 (17%)
Prior PCI of any vessel (%)	8 (35%)
Prior stroke (%)	0 (0%)
Left ventricular ejection fraction (%)	67% (55–75%)
Number of vessels	26
Left anterior descending	17
Left circumflex	5
Right coronary artery	2
Ramus intermedius	2
FFR	0.81 ± 0.08

Note: Summary values represent number (%), mean ± SD, or median (interquartile range, IQR).
Abbreviations: FFR, fractional flow reserve; PCI, percutaneous coronary intervention.

2.3 | Statistical methods

Analyses were performed using R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria). We employed standard statistical techniques. Applicable tests were two-tailed, and $p < .05$ was considered statistically significant. ANOVA from a linear mixed effects model with random effects within subjects assessed each of five parameters among pre-equalization, post-equalization, and drift check tracings. If this ANOVA was significant, then a pair-wise t-test comparison with Bonferroni correction was performed to determine which tracings differed.

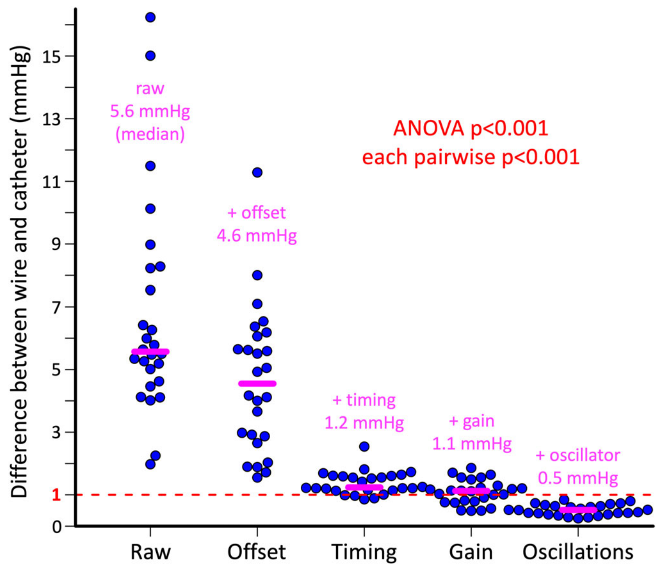

FIGURE 3 Sequential improvement in matching fluid-filled catheter and pressure wire. For 26 coronary lesions from 23 subjects, the root mean square (RMS) difference between aortic pressures measured with a 0.014″ high-fidelity pressure wire and fluid-filled guide catheter fell with sequential corrections mirroring the example in Figure 2. Matching the average pressure offset and adjusting for timing provided the largest absolute improvements. However, additional adjustments for differential gain as well as the harmonic oscillator behavior of the fluid-filled system brought the median RMS well below 1 mmHg. Repeated measures ANOVA detected a systematic difference ($p < .001$) among corrections, with each paired t test demonstrating a significant reduction in the RMS value ($p < .001$) even after Bonferroni correction [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Fit parameters and stability for coronary corrections, ordered by drift

		Offset (mmHg)		Temporal shift[a]		Gain[a]		Frequency (Hz)		Damping[a]	
Case	Sequence	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD
9	Start	7.8	0.27	−9.4	0.11	1.082	0.0069	9.1	0.14	0.38	0.011
	Equalized	−5.3	0.21	−9.6	0.08	1.068	0.0021	8.9	0.11	0.38	0.007
	Pullback	−17.4	0.15	−9.4	0.06	1.088	0.0017	9.2	0.10	0.38	0.007
3	Start	1.8	0.34	−8.2	0.18	1.027	0.0083	8.5	0.15	0.35	0.022
	Equalized	−3.2	0.23	−8.2	0.14	1.051	0.0107	8.3	0.20	0.41	0.019
	Pullback	−5.8	0.21	−8.3	0.13	1.052	0.0071	8.7	0.15	0.39	0.013
11	Start	3.0	0.20	−8.9	0.14	1.036	0.0112	27.9	1.89	0.48	0.046
	Equalized	−1.8	0.20	−8.9	0.15	1.021	0.0024	26.2	1.19	0.48	0.039
	Pullback	−3.6	0.91	−9.1	0.36	1.022	0.0060	22.2	3.22	0.76	0.078
14	Start	5.6	0.24	−5.2	0.14	0.969	0.0038	10.7	0.19	0.15	0.020
	Equalized	1.8	0.40	−4.9	0.16	0.978	0.0034	11.0	0.23	0.15	0.019
	Pullback	0.0	0.23	−8.7	0.11	1.019	0.0029	5.8	0.03	0.38	0.009
21	Start	−3.5	0.49	−5.2	0.14	1.047	0.0055	6.5	0.07	0.32	0.011
	Equalized	−3.8	0.43	−5.3	0.19	1.040	0.0046	6.4	0.07	0.35	0.009
	Pullback	−5.6	0.32	−5.2	0.17	1.055	0.0093	6.4	0.09	0.30	0.022
5	Start	1.9	0.28	−8.9	0.21	1.018	0.0080	12.7	0.56	0.45	0.018
	Equalized	−2.2	0.23	−9.0	0.14	1.032	0.0031	12.9	0.25	0.42	0.019
	Pullback	−3.8	0.17	−9.0	0.19	1.029	0.0021	14.1	0.52	0.64	0.019
1	Start	−2.7	0.40	−5.8	0.29	1.075	0.0088	26.9	3.45	0.74	0.047
	Equalized	−5.4	0.39	−5.9	0.23	1.065	0.0021	29.4	2.81	0.74	0.043
	Pullback	−6.8	0.23	−6.0	0.23	1.075	0.0064	27.0	2.34	0.73	0.030
4	Start	2.2	0.74	−9.4	0.25	1.084	0.0145	15.0	1.00	0.40	0.048
	Equalized	−9.7	0.31	−9.2	0.19	1.077	0.0029	15.3	0.44	0.37	0.042
	Pullback	−10.9	0.25	−9.6	0.23	1.063	0.0024	15.4	0.48	0.45	0.052
6	Start	6.4	0.36	−8.1	0.21	1.004	0.0021	16.0	0.49	0.31	0.054
	Equalized	−0.3	0.17	−8.2	0.30	1.000	0.0022	15.6	0.43	0.31	0.069
	Pullback	−1.4	0.22	−8.2	0.32	1.007	0.0021	15.8	0.82	0.25	0.057
7	Start	−3.9	0.22	−7.8	0.25	1.036	0.0034	14.5	0.70	0.23	0.057
	Equalized	−2.5	0.26	−8.1	0.29	1.036	0.0044	14.2	0.48	0.26	0.050
	Pullback	−3.3	0.38	−8.5	0.41	1.029	0.0053	14.1	0.74	0.45	0.058
18	Start	−3.4	0.15	−8.6	0.27	1.034	0.0017	28.5	5.51	0.28	0.177
	Equalized	−2.1	0.18	−8.4	0.24	1.035	0.0020	29.2	5.30	0.25	0.150
	Pullback	−2.9	0.20	−8.5	0.28	1.039	0.0027	29.9	6.78	0.28	0.168
16	Start	−9.4	0.44	−9.7	0.13	1.055	0.0025	13.9	0.60	0.65	0.030
	Equalized	−7.3	0.19	−9.8	0.09	1.083	0.0021	15.0	0.31	0.48	0.015
	Pullback	−7.9	0.17	−9.5	0.21	1.087	0.0113	14.9	0.55	0.43	0.047
19	Start	−6.4	0.42	−9.1	0.46	1.093	0.0092	15.7	2.42	0.35	0.096
	Equalized	−3.8	0.18	−9.4	0.27	1.079	0.0027	14.6	0.76	0.36	0.071
	Pullback	−4.3	0.29	−9.2	0.35	1.086	0.0026	16.1	1.48	0.34	0.086
26	Start	5.9	0.39	−4.7	0.29	1.092	0.0120	12.8	0.38	0.35	0.036
	Equalized	−5.0	0.23	−4.5	0.22	1.081	0.0028	13.0	0.27	0.33	0.030
	Pullback	−5.5	0.23	−4.2	0.12	1.087	0.0033	13.6	0.24	0.27	0.014
25	Start	−2.0	0.41	−5.0	0.10	1.077	0.0264	11.6	0.45	0.37	0.043
	Equalized	−6.6	0.26	−5.0	0.16	1.071	0.0031	11.3	0.15	0.38	0.024
	Pullback	−6.9	0.63	−5.3	0.26	1.056	0.0150	13.3	1.28	0.40	0.049

(Continues)

TABLE 2 (Continued)

Case	Sequence	Offset (mmHg) Median	Offset (mmHg) SD	Temporal shift[a] Median	Temporal shift[a] SD	Gain[a] Median	Gain[a] SD	Frequency (Hz) Median	Frequency (Hz) SD	Damping[a] Median	Damping[a] SD
12	Start	−4.5	0.79	−7.5	0.19	1.019	0.0109	18.6	1.11	0.08	0.019
	Equalized	−1.2	0.62	−7.5	0.13	1.007	0.0064	19.0	0.73	0.10	0.029
	Pullback	−1.5	0.81	−7.7	0.21	1.015	0.0070	19.8	1.18	0.10	0.054
2	Start	−1.6	0.18	−4.8	0.11	0.979	0.0023	13.8	0.21	0.11	0.010
	Equalized	1.7	0.18	−4.9	0.13	0.982	0.0023	14.1	0.32	0.12	0.012
	Pullback	1.9	0.34	−4.0	0.20	0.970	0.0040	13.8	0.36	0.09	0.021
24	Start	−2.1	0.23	−10.3	0.18	1.071	0.0117	11.1	0.54	0.55	0.023
	Equalized	−6.0	0.31	−10.6	0.21	1.061	0.0027	10.4	0.47	0.54	0.029
	Pullback	−5.7	0.16	−10.7	0.11	1.061	0.0016	9.6	0.14	0.51	0.019
20	Start	−3.1	1.28	−5.3	0.21	1.058	0.0101	6.4	0.10	0.32	0.024
	Equalized	−2.2	0.54	−5.2	0.08	1.040	0.0057	6.4	0.08	0.37	0.012
	Pullback	−1.8	0.42	−5.3	0.14	1.067	0.0177	6.5	0.09	0.31	0.018
10	Start	−7.3	0.37	−10.0	0.25	1.075	0.0174	19.5	1.77	0.70	0.049
	Equalized	−4.3	0.23	−10.2	0.22	1.054	0.0028	18.4	0.74	0.70	0.038
	Pullback	−3.8	0.60	−10.2	0.21	1.087	0.0232	18.6	0.82	0.74	0.025
15	Start	−9.7	0.60	−9.5	0.32	1.097	0.0097	14.6	1.16	0.43	0.039
	Equalized	−6.7	0.38	−9.5	0.17	1.088	0.0030	14.3	0.50	0.42	0.035
	Pullback	−6.0	0.40	−9.5	0.13	1.087	0.0129	15.2	0.89	0.41	0.036
23	Start	−1.1	0.28	−5.1	0.12	1.093	0.0147	9.1	0.14	0.38	0.009
	Equalized	−6.4	0.17	−5.2	0.08	1.081	0.0021	8.9	0.13	0.39	0.005
	Pullback	−5.4	0.16	−5.1	0.08	1.076	0.0045	9.2	0.14	0.39	0.017
22	Start	−1.4	0.17	−10.7	0.07	1.087	0.0091	16.3	0.21	0.76	0.008
	Equalized	−5.5	0.16	−10.8	0.09	1.077	0.0017	16.1	0.74	0.70	0.023
	Pullback	−4.3	0.15	−10.4	0.26	1.077	0.0031	16.0	1.35	0.66	0.035
17	Start	−2.1	0.61	−8.0	0.26	1.032	0.0152	30.5	10.89	0.45	0.193
	Equalized	−4.6	0.41	−8.3	0.23	1.050	0.0031	25.0	1.55	0.34	0.079
	Pullback	−2.9	0.49	−8.9	0.20	1.052	0.0130	32.1	5.68	0.48	0.156
8	Start	−1.9	0.25	−9.2	0.12	1.074	0.0096	13.2	0.33	0.43	0.020
	Equalized	−5.0	0.21	−9.4	0.08	1.067	0.0018	12.5	0.15	0.41	0.010
	Pullback	−3.3	0.13	−9.6	0.10	1.071	0.0022	12.1	0.17	0.43	0.020
13	Start	−8.7	1.04	−9.5	0.25	1.115	0.0118	17.6	1.33	0.56	0.058
	Equalized	−8.4	0.40	−9.2	0.32	1.097	0.0051	16.7	1.02	0.40	0.071
	Pullback	−6.4	0.45	−9.0	0.30	1.119	0.0304	20.7	3.15	0.54	0.104

[a]Temporal shift has units of samples (240/s), while gain and damping are unitless.

3 | RESULTS

We studied 26 coronary lesions in 23 subjects with clinical characteristics as summarized in Table 1. The number of valid, analyzed beats was 40 ± 9 for each of the three approximate 30 s segments (pre-equalization, post-equalization, and pullback drift check) of simultaneous aortic pressure from the pressure wire and catheter. On average four beats were rejected from each tracing, generally due to their occurrence at the start or end of the recording with resulting incomplete cardiac cycles and pressure averaging.

3.1 | Matching aortic tracings

Figure 3 displays the RMS error between the pressure wire and fluid-filled catheter for progressive, step-wise corrections as in Figure 2. Compared to the raw tracing median RMS error of 5.6 mmHg, matching the average pressure offset decreased the median error to 4.6 mmHg, and adjusting for timing shift further decreased median error to 1.2 mmHg. These two steps provided the largest absolute improvements. However, additional adjustments for differential gain (median error decreased further to 1.1 mmHg) as well as the harmonic

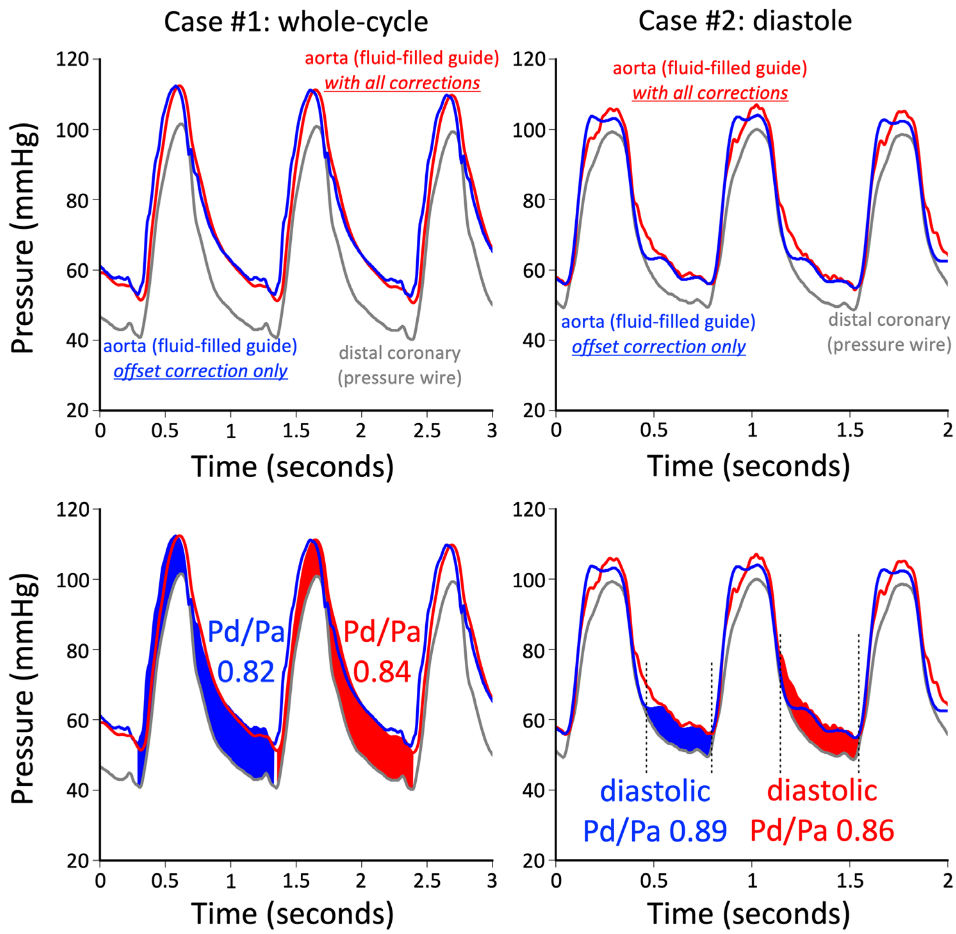

FIGURE 4 Impact of catheter correction on coronary pressure assessment. Correcting the guide catheter pressure to match the pressure wire improves subsequent measurements in the coronary vessels. Colors are used differently in this figure, since the fully corrected catheter pressure provides the best reference (shown in red here like the wire in Figure 2) and the catheter with only offset correction shown in blue (similar to the partially corrected tracings in Figure 2). Gray rather than red for the pressure wire indicates its distal location, and filled color highlights the pressure difference. As quantified in the main text, whole-cycle coronary FFR measurements (example on left) demonstrated a smaller impact than diastolic measurements (example on right) when additionally corrected for timing, gain, and oscillations. The example on the left shows a large 0.02 impact on whole-cycle Pd/Pa (here, FFR since tracing was made during hyperemia) after correcting the aortic pressure, mainly due to timing. The example on the right shows a large 0.03 change in diastolic Pd/Pa after correcting the aortic pressure, mainly due to suppression of oscillations that shift the apparent onset of diastole [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Available implementations to match pressure wire with guide catheter

	Offset	Timing	Gain	Harmonic oscillator
Abbott Vascular	X	X		
Philips Volcano	X	X		
Boston Scientific	X			
Opsens Medical			X	
Current manuscript	X	X	X	X

oscillator behavior of the fluid-filled system brought the median error to 0.52 mmHg after all 5 model parameters were included.

Repeated measures ANOVA detected a systematic difference ($p < .001$) among corrections, with each paired t test demonstrating a significant reduction in the RMS error ($p < .001$) after Bonferroni correction. Adding a second harmonic oscillator did not provide significant further improvement (median error 0.51 mmHg, paired p value .552). For cases with ≤1 mmHg pressure drift at pullback after 5-parameter equalization, the median error value rose from 0.51 mmHg post-equalization to 0.99 mmHg during drift check (uncorrected paired p value .002). These results quantify that, in the absence of significant drift, more than half of fluid-filled catheters can be corrected and maintained to within 1 mmHg RMS error versus a pressure wire throughout a typical FFR measurement.

3.2 | Parameter variation

Table 2 summarizes the 5-parameter values for every lesion during pre-equalization, post-equalization, and pullback drift check. Pressure offset demonstrated an expectedly different value among the three tracings (ANOVA p = .003) since the hemodynamic console performed average pressure equalization. Pairwise t testing confirmed a significant change in pressure offset from pre-equalization to post-equalization (p = .034) and to drift check (p = .046), but no significant difference between post-equalization and drift check (p = .455). In contrast to these variations in pressure offset, the parameters for timing (ANOVA p = .304), differential gain (ANOVA p = .105), harmonic oscillator frequency (ANOVA p = .677), and harmonic oscillator damping (ANOVA p = .137) did not change significantly among pre-equalization, post-equalization, and drift check tracings. Thus all correction parameters remain stable during a typical FFR measurement with the exception of pressure offset due to the well-known drift effect.

The row entries in Table 2 have been sorted by the magnitude in pressure offset change between post-equalization and drift check from largest (12.1 mmHg drift) to smallest (0.5 mmHg). Other than the 12.1 mmHg outlier, the other 25 lesions had a pressure drift of <3 mmHg, and only 1 other case (2.6 mmHg) had a pressure drift >2 mmHg. In 13 of the 26 cases (50%), the pressure drift was ≤1 mmHg. Temporal shift values in Table 2 remained uniformly negative, implying that the uncorrected aortic pressure from the fluid-filled catheter leads the pressure wire for this catheterization laboratory setup. For 24 of the 26 cases (92%), differential gain consistently reached >1.0, indicating that the manifold transducer for the fluid-filled catheter generally responded relatively less to pressure changes compared with the pressure wire.

For the harmonic oscillator parameters, a significant but weak, direct correlation existed between frequency and the damping factor (Pearson r = 0.247, 95% confidence interval 0.026 to 0.445, p = .029). For 22 of the 26 oscillators (85%), the oscillator frequency parameter was <20 Hz. Our model considered only underdamped ("ringing") systems (technically a damping factor < 1, as shown in Table 2).

3.3 | Impact on coronary stenosis tracings

Comparing whole-cycle FFR values between standard pressure offset equalization and our 5-parameter equalization yielded an average difference of +0.006 (95% confidence interval −0.016 to +0.028), coefficient of variation 1.3%, and paired p value .017. Comparing diastolic FFR values produced an average difference of +0.007 (95% confidence interval −0.022 to +0.035), coefficient of variation 1.9%, and paired p value .026. The supplement provides Bland–Altman plots. While the 5-parameter equalization changed both whole-cycle and sub-cycle pressure ratios, the magnitude of correction for diastolic FFR exceeded that for whole-cycle FFR (paired p = .0016).

As can be seen in Figure 4, some lesions displayed a marked impact from 5-parameter equalization. The tracing in the left panel shows a 0.02 difference for whole-cycle FFR—the fifth largest in the cohort—after correcting the aortic pressure, mainly due to timing. The lesion on the right shows a large 0.03 change in diastolic FFR—the third largest in the cohort—after correcting the aortic pressure, mainly due to suppression of oscillations that shift the apparent onset of diastole.

4 | DISCUSSION

When recording phasic aortic pressure as part of a coronary or valve study, fidelity is key for accurate physiologic assessment. Given that invasive physiology often acts as the final gatekeeper for coronary revascularization or valve implantation, a biased or faulty measurement can lead to adverse clinical consequences when accounting for the periprocedural risk of any device therapy. Ideally a second pressure wire would be inserted to measure aortic pressure,[2] in addition to the existing pressure wire in the distal coronary artery or left ventricle. However, its added cost and logistical complexity remain prohibitive in daily practice.

Our novel software algorithm extracts extra information during the standard equalization performed between the fluid-filled guide catheter and 0.014″ pressure wire. The results show that phasic aortic signals can be matched within 1 mmHg root mean square error, and this high level of agreement is maintained during typical clinical assessments. Unlike existing algorithms that mainly focus on static pressure offset (equivalent to raising or lowering the height of the manifold transducer), we additionally account for timing differences (due to catheter pressure propagation delay, electronic delays or signal processing), differential gain (between the manifold transducer and pressure wire sensors), and harmonic oscillator behavior of the fluid-filled catheter. Together, these factors improve the fidelity of the aortic signal—almost as if using a second pressure wire "for free"—without extra effort by the operator who can proceed with the diagnostic procedure in usual fashion. Practically, existing hemodynamic console software could be upgraded by incorporating our algorithm to improve fidelity without any change to the pressure sensor or other hardware.

At the moment, heterogeneity exists among pressure wire manufacturers regarding the proper technique for equalizing aortic pressures. As detailed in Table 3, some systems account only for pressure offset, while others simultaneously correct for timing differences as well. Still other systems incorporate only differential gain. Our study clarifies in Figures 2 and 3 that all of these mechanisms are important to match phasic aortic pressures, but still neglect the harmonic oscillator behavior of fluid-filled systems. While oscillations were appreciated for decades,[9] data processing for correction was not available. By using the piezoelectric or fiberoptic pressure wire as the reference—strangely the opposite of current practice despite its greater pressure fidelity and superior frequency response—we have developed an automatic method to quantify and adjust for these oscillations.

In some cases, vigorous flushing of the fluid-filled catheter can diminish the "ringing" by removing bubbles or debris. Indeed, our automatic algorithm provides a quantitative method to alert the operator that further flushing could be beneficial in situations with a low-frequency oscillator and a small damping factor. Because meticulous attention was paid to these matters during this protocol, our results probably represent a "best case" scenario with minimized harmonic oscillator components. While a guiding catheter by itself can have a relatively high natural frequency, the addition of stopcocks, extension tubing, and manifold create a unique aggregate with a complex frequency response.[13] Nevertheless, Figure 2 indicates that our 5-parameter model captures most of the details with no further benefit seen by adding a second harmonic oscillator.

Although the average change in whole-cycle versus diastolic coronary pressure ratios remained <0.01, outliers exist like the examples in Figure 4. In certain cases, changes of 0.02–0.03 in FFR or NHPR will lead to a different clinical decision regarding treatment, although guidelines have begun to distinguish between an FFR of 0.75 as prognostically relevant and 0.80 as hemodynamically relevant.[14] Because 5-parameter equalization introduces larger differences for diastolic FFR versus whole-cycle FFR, we would expect the same results to hold for subcycle NHPR depending on the definition of the subcycle and relative contributions of the five parameters, since oscillations impact diastole less than systole. Thus resting physiology not only has an inferior test/retest repeatability compared to hyperemia,[15] but also remains relatively more sensitive to factors like hydrostatic pressure[16] and catheter equalization during diastole (this study). Our novel equalization algorithm provides a method for reducing the last of these 3 factors that make NHPR less precise.

4.1 | Comparison to existing literature

A wide literature has examined the frequency response characteristics of fluid-filled catheters since the advent of modern physiologic recording systems approximately 60 years ago.[9] The technique of Fourier analysis to characterize and eliminate frequency-dependent distortions—originally suggested for cardiovascular pressure assessment in 1928—requires an impulse-response technique (so-called "pop" or "snap" test) less suitable for in vivo application as well as a reference manometer device.[13] Our method replaces the manometer-tipped catheter with a more readily available commercial pressure wire. Additionally, we do not require a "pop" test but instead use signal processing of the phasic aortic pressure wire recording as a natural reference. By fixing the transfer function to take the shape of a damped harmonic oscillator, we overcome the limited frequency components inherent in a relatively stable heart rate. To our knowledge, this combination of 0.014″ pressure wire and 5-parameter model to match phasic aortic pressures using a limited number of cardiac cycles under routine clinical conditions has not been described previously.

The drift performance of commercial pressure wires[17] has previously focused only on offset without taking into consideration the other factors depicted in Figure 2. Consider a wire and guide catheter system that performs with a gain factor of 1.09 like case #19 in Table 2. Although both traditional offset-only equalization and our 5-parameter equalization will produce identical average pressure values at baseline, if a drift check is performed after a fall in blood pressure—as commonly occurs with intravenous adenosine hyperemia—then the apparent drift equals $(1.09–1.00) \times \Delta Pa$, where ΔPa indicates the change in aortic pressure between equalization and pullback. Thus offset-only equalization would incorrectly show a drift of $0.09 \times 30 = 2.7$ mmHg if the mean aortic pressure decreased from 95 to 65 mmHg—not uncommon for intravenous adenosine; in actuality, the wire had no drift at all. Note that this example neglects other factors accounted for by our 5-parameter equalization like timing differences and oscillations. As a result, our equalization algorithm has the potential to improve the apparent drift performance of existing pressure wires without any change in material or sensor design.

4.2 | Limitations

Some catheter systems may have more complex frequency responses than allowed by our 5-parameter model as suggested by prior work.[13] Additionally, our "gold standard" pressure wire itself has a frequency response that remains flat only until about 25 Hz.[8] Therefore, more sophisticated models and higher-fidelity pressure sensors might allow for superior matching beyond the <1 mmHg RMS error in Figure 3, although such sensors are not available for routine clinical procedures. Because meticulous attention was paid to the fluid-filled aortic waveform, our cohort avoided so-called "ventricularized" tracings and other distortions.[17] We recommend equalization using high-quality aortic waveforms for both fluid-filled catheter and pressure wire since the impact of distortion on our 5-parameter equalization remains uncertain. While we did not measure NHPR directly, our analysis and Figure 4 would be expected to hold regardless of the size of gradient. Finally, our algorithm was applied post hoc instead of real time and the sample size was modest given the rigorous physiologic protocols and setup.

5 | CONCLUSION

When calibrating phasic aortic pressure signals from a fluid-filled catheter using a pressure wire as reference, correction requires five parameters: offset, timing, gain, and oscillations (frequency and damping factor). Our novel algorithm improves the fidelity of the aortic signal—almost as if using a second pressure wire "for free"—without extra effort by the operator who can proceed with the diagnostic procedure in usual fashion. The impact of correction was larger for subcycle versus whole-cycle metrics, indicating a key role for valvular stenosis and subcycle coronary pressure ratios. Automatically eliminating common errors may improve some clinical decisions regarding physiology-based intervention.

CONFLICT OF INTERESTS

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, RLK, BDB, KLG, and NPJ have a patent pending on the correction algorithm described in this manuscript. SF received general support from the Swiss National Science Foundation the Fondation Vaudoise de Cardiology. RLK reports no additional support or industry relationships. BDB has received institutional research grants and consulting fees from Abbott Vascular (formerly St. Jude Medical), Boston Scientific, and Opsens. KLG is the 510(k) applicant for CFR Quant (K113754) and HeartSee (K143664 and K171303), 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 and consulting agreement with Boston Scientific for the smart minimum FFR algorithm.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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