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Effect of arterial pressure measurement location on pulse contour stroke volume estimation, during a rapid change in hemodynamic state

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Abstract: Continuous cardiac output monitors are becoming more common in clinical settings to assess cardiac performance. Pulse contour analysis is a common method employed by commercial devices to estimate patient hemodynamics from a pressure waveform and relate it to volume. The main issue with current devices, is they can perform poorly during and after a significant hemodynamic event. An existing pulse contour analysis method, under ideal experimental conditions, demonstrated the ability to track changes in stroke volume (SV) using a measure of pulse wave velocity (PWV). In this study, the existing method's ability to estimate SV was tested during vena cava occlusions (VCO), a *worst case*, rapid transient hemodynamic change. Additionally, the method's sensitivity to the location of the arterial pressure waveform measurement was also assessed, by comparing SV estimates from aortic and iliac pressures, to SV measured by admittance catheter in the ventricle. Results show the model accurately tracks changes in SV as a result of the occlusion, a significant improvement over current commercially available devices. Bland-Altman analysis showed no significant improvement in SV estimation when using aortic pressure compared to the iliac pressure waveform, with mean bias of -2.11ml and 0.13ml, respectively. This is a desirable result, as more distal arterial pressure measurement locations increase the clinical feasibility of the method.

Keywords: Cardiovascular system, stroke volume, model, biosignals, signal processing

1. INTRODUCTION

Stroke volume (SV) measures are useful clinically for diagnosis and treatment of a range of cardiovascular dysfunctions (Reuter et al., 2003; Luecke and Pelosi, 2005; Montenij et al., 2011). By measuring SV continuously, beat to beat, patient response to treatment or changes in disease state can be provided to clinicians, optimising care (Tibby, 2003; Cecconi et al., 2014; Marik, 2013).

Pulse contour analysis is one method of determining SV and/or cardiac output (CO). CO is just the multiple of SV and heart rate, giving the flow over time, rather than per beat. Pulse contour analysis, relies on the general understanding that pressure drives flow. Hence, the methods seek to infer parameters representative of a patients specific hemodynamic state from an arterial pressure waveform and calculate an estimated SV.

There are currently three commercially available continuous cardiac output (CO) monitors that use pulse contour analysis, FloTrac™ (Edwards Lifesciences, USA), PiCCO (Pulsion Maquet Getinge Group, Germany) and esCCO (Nihon Kohden®). Each is limited by their inability to accurately measure stroke volume following a hemodynamic change, unless recalibration is performed (Marik, 2013; Goedje et al., 1999; Rödig et al., 1999; Obata et al., 2017; Bataille et al., 2012; Hadian et al., 2010). This issue makes them unsuitable for patients who could benefit most from monitoring, those likely to experience sudden and unpredictable hemodynamic changes as a result of both treatment and disease progression.

Kamoi et al. (2017) overcame these limitations by developing a model whose parameters were dependent on pulse wave velocity (PWV). By monitoring changes in PWV Kamoi et al. (2017) showed the possibility of estimated SV during both steady state and transient hemodynamic behaviour. However, the methods sensitivity to arterial pressure measurement location is unknown.

The method is based on *the reservoir wave approach* (Tyberg et al., 2014), where reservoir refers to the blood associated with the expansion of the aorta. The aorta is more compliant than distal arteries (Nichols et al., 2011), and thus it is possible the reservoir wave approach assumptions are less applicable to distal arterial pressure signals. This issue could lead to poorer SV estimation.

Additionally, this method requires identification of the transition from systole to diastole on the pressure waveform. More centrally located arterial pressure signals have

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clear dicrotic notches, making identification of end systole easier. A distal arterial pressure signal can have no clear dicrotic notch (Dawber et al., 1973), hence, SV estimates derived from such signals may be less accurate.

This study compares SV estimates using aortic and iliac artery pressure waveforms. The motivation is to improve the clinical applicability of the method, as in a clinical setting, the location of arterial pressure catheters can vary (Gershengorn et al., 2014). If the method works for a range of arterial pressure locations, the method is more clinically applicable.

2. METHODS

2.1 Stroke volume estimation method

The existing Kamoi model method showed the clinical potential and capacity of model-based, beat-to-beat stroke volume estimation (Kamoi et al., 2017). One limitation was the inaccurate arterial pressure catheter spacing, due to two individual pressure catheters being used. In this experiment, the limitation is overcome using a dual sensor catheter allowing accurate PWV measurements.

Current clinically available SV and CO estimates are limited in accuracy following hemodynamic instability (Marik, 2013; Goedje et al., 1999; Philips Electronics North America Corporation, 2002; Rödig et al., 1999; Obata et al., 2017; Bataille et al., 2012; Hadian et al., 2010). Kamoi et al. (2017) attempted to overcome this issue through beat to beat dynamic calibration of model parameters by monitoring PWV. Specifically, Kamoi et al. (2017) used the Bramwell-Hill and water hammer equations to relate PWV to arterial compliance (C) and impedance (Z). This experiment assesses model accuracy on a different hemodynamic modification using a non-aortic arterial pressure measurement, which maybe more clinically accessible.

A detailed description of the method is discussed elsewhere (Kamoi et al., 2017). A summary of the main equations, applied assuming the start of each heart beat is t=0, is defined:

$$P_{res}(t) = e^{-(\alpha+\beta)t}\left(\int_0^t \left[e^{(\alpha+\beta)\tau}(\alpha P_m(\tau) + \beta P_{cvp}(\tau))\right]d\tau + P_m(0)\right) \quad (1)$$

where, P_{res} is reservoir pressure, P_m is the measured arterial pressure, P_{cvp} is the central venous pressure, α is PWV/L_{art} and β is $1/RC$. L_{art} refers to the characteristic length of the artery and R the peripheral resistance.

$$P_{ex}(t) = P_{mea}(t) - P_{res}(t) \quad (2)$$

where P_{ex} is known as the excess pressure associated with systole (since during diastole $P_{mea} = P_{res}$).

Finally, the SV estimate comes from:

$$SV_{est} = \frac{1}{Z}\int_0^{t_d} P_{ex}(t)dt \quad (3)$$

where t_d refers to the time of end systole or start diastole, since during diastole excess pressure should be zero.

2.2 Porcine trials and measurements

Data in this study was provided by pig experiments at the Centre Hospitalier Universitaire de Liège, Belgium. Ethics approval for the experimental procedures, protocols and use of the data was provided by the Ethics Committee of the University of Liège Medical Faculty.

Five pure Pietrain pigs were used in the experiments. Pigs were administered ketamine (20 mg/kg) and diazepam (1 mg/kg) prior to the experiment. Anaesthesia was induced and maintained by continuous infusion of sufentanil (0.5 µg/kg/h) and sodium pentobarbital (3 mg/kg). Pigs were intubated via tracheotomy and ventilated using a Engström Carestation ventilator (GE, Madison, WI, USA). The ventilator was set to a tidal volume of 10ml/kg, an O2 inspired fraction of 0.5, a respiratory frequency of 20 respirations per minute and a PEEP (Positive End-Expiratory Pressure) of 5 cmH_2O.

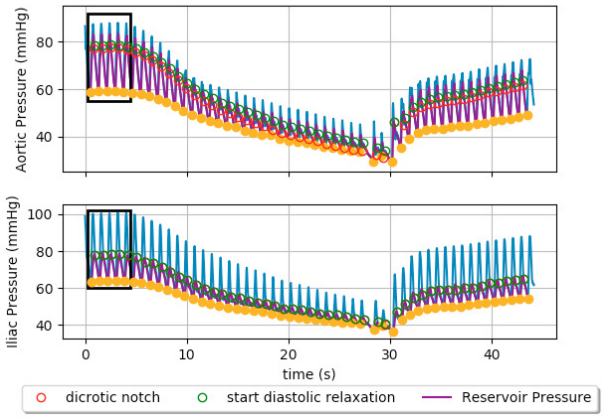
Pressure and volume were directly measured in the left ventricle using a 5F micromanometer-tipped admittance catheter (Transonic, Ithaca, NY, USA) inserted into the ventricle through the right carotid artery. A single lumen pressure sensor (Transonic, Ithaca, NY, USA) was also located in the inferior vena cava, along with a Forgarty balloon used to modify ventricle preload (Sato et al., 1998).

A 7F dual sensor pressure catheter, with 40cm sensor spacing was introduced via the femoral artery (Transonic, Ithaca, NY, USA). The upper sensor was located in the aortic arch, meaning the second sensor was approximately in the iliac arteries. Knowledge of the exact sensor spacing allows for accuarate pulse wave velocity (PWV) measurements. All data were sampled at 250Hz.

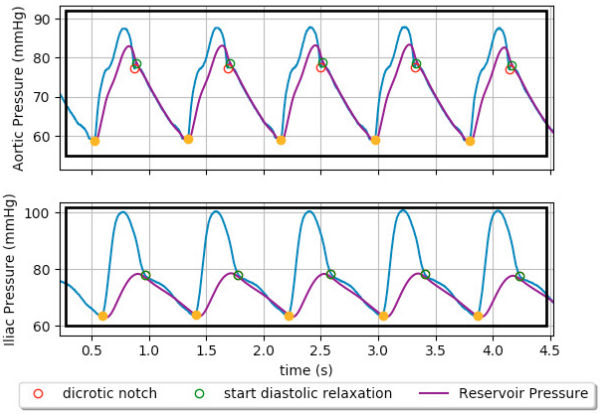
2.3 Hemodynamic modification

Baseline data was recorded prior to hemodynamic modification and it's duration ranged from 93 beats (Pig 4) to 317 beats (Pig 2). The first 10 beats of the baseline state are used to calibrate the model by using the SV measured from the admittance catheter for each beat. With this SV measurement, model parameters Z and C, as well as the aortic area (A) and a characteristic length (L), are calculated. L is assumed to remain constant throughout the experiment, while other model parameter variation was captured through PWV, as explained in Kamoi et al. (2017). Following calibration, SV was estimated for the remainder of the baseline heart beats, verifying model performance at steady state.

Following baseline, a vena cava occlusion (VCO) was performed by inflating the Forgarty balloon. Pig 5 received two VCOs and both were used in the analysis. VCO reduces the flow of blood to the right ventricle, which subsequently reduces blood flow to the left ventricle, leading to an eventual fall in ejection and SV (Van Der Velde et al., 1991). Additionally, the reduction in returning blood to the ventricles causes a fall in preload and afterload (Sato et al., 1998; Newlin and Levenson, 1979). To remove the effects of breathing on the circulatory system (Westphal et al., 2006), the ventilator was turned off during the VCO.



(a) Aortic and iliac pressure waveforms during VCO and respective reservoir pressure waveforms.



(b) Zoomed view of aortic and iliac pressure waveforms showing reservoir pressure fit.

Fig. 1: A typical example of the aortic and iliac pressure waveforms during VCO for Pig 2, whose SV estimates had the lowest accuracy. Note the iliac pressure waveform has no distinct turning point type dicrotic notches.

While this event is unlikely in the intensive care unit, it does represent a *worst case* scenario for testing the SV model. This is because the event is transient, with the sudden inflation of the balloon causing occlusion. Balloon inflation and subsequent deflation lasted between 36 (Pig 1) and 60 beats (Pig 3). If SV estimation can track changes in directly measured SV during this hemodynamic change, without needing recalibration from the baseline case, then it is an improvement over existing clinical continuous SV estimation devices.

3. RESULTS

Figure 1 shows typical aortic and iliac pressure signal response to a VCO. Specifically, the figure is for Pig 2. The stroke volume waveform for each pig is shown in Figure 2, while Bland-Altman plots are shown in Figure 3 to provide quantitative measures of the estimates agreement.

With the exception of Pig 3, the mean absolute percentage error for the initial baseline heart beats was less than 12.4% for all pigs. This error came from Pig 2's iliac based SV estimate and represents a mean error of 4.5ml from the 35.1ml baseline. However, Pig 3 had a mean absolute percentage error of 40.1%. This error can be attributed to a poor quality admittance catheter ventricle volume signal, combined with a relatively low baseline stroke volume. Pig 3's mean SV during baseline was 26.1ml, with standard deviation of 8.2ml (coefficient of variation 31.4%), while the model based estimates for both the aortic arch and iliac based SV estimates were consistent at a mean of 29.4ml and standard deviation of 3ml and 2.3ml respectively. Thus, in this pigs case, the model based estimate may in fact represent a more accurate measure, although there was no way to verify this.

Despite the offset between Pig 3's baseline measured and estimated SV, changes in SV are still useful clinically for monitoring disease state and treatment efficacy (Marik, 2013). As can be seen from Figure 2 (c), the model trends the measured SV during the VCO well.

4. DISCUSSION

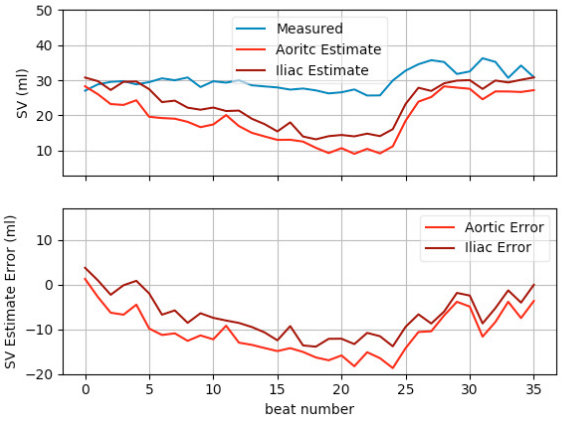
4.1 SV Waveforms

Figure 2 shows all pigs SV estimates fell, due to the model's dependency on arterial pressure, which fell during the VCO. Figures 2 (c-f), show successful response of the model estimated SV in capturing the change in measured SV. It is also clear, in these two cases, the aortic arch pressure based SV estimate performed no better than the downstream iliac pressure based SV estimate.

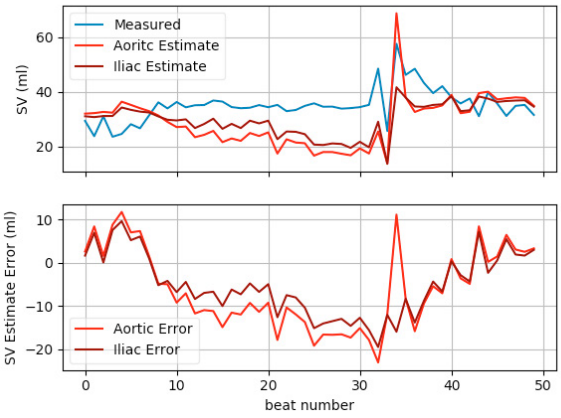
No change in performance between these two SV estimates may seem surprising for two reasons. First, the presence of the dicrotic notch in the aortic arch signal suggests more accurate detection of end systole, the point where $P_{excess} = 0$. With no dicrotic notch present in the iliac signal, end systole is much more difficult to determine. However, (Balmer et al., 2018) presents the improved end systole estimation technique used in this study.

Despite the end systolic time being easier to detect in the aortic pressure waveform, the mechanisms leading to the dicrotic notch are not accounted for in the model. Thus, the reservoir pressure waveform does not take into account the effect of complex valve closure dynamics on the measured pressure in the aorta. Since the iliac signal does not typically contain turning point type dicrotic notches, its waveform conforms closer to the model assumptions.

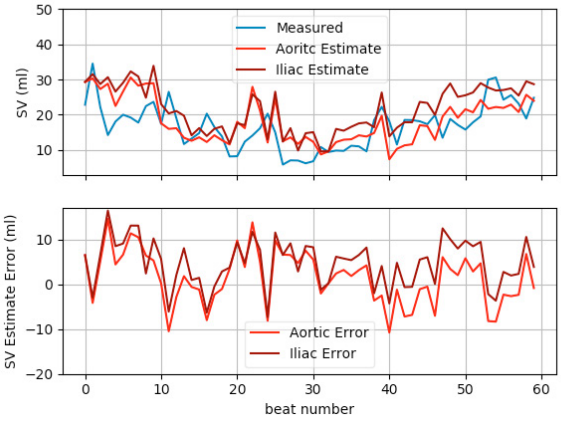
Second, it is well known that the compliance of the arterial tree reduces further from the heart (Nichols et al., 2011). Given the method's basis on the windkessel model, and thus it's reliance on arterial compliance (Kamoi et al., 2017), it was suspected distal arteries would not represent the blood storage component ($P_{reservoir}$) of the aorta adequately enough for a good SV estimate. However, Figures 2 (c-f) suggest the iliac pressure waveform performs equally well as the aortic pressure waveform. The reason, is the model parameters are found in a way that reinforces assumed physiology. Specifically, the parameter identifica-



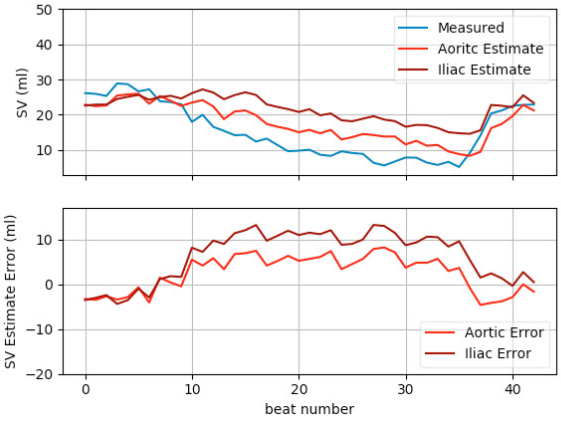
(a) Pig 1 VCO SV measure and estimates.



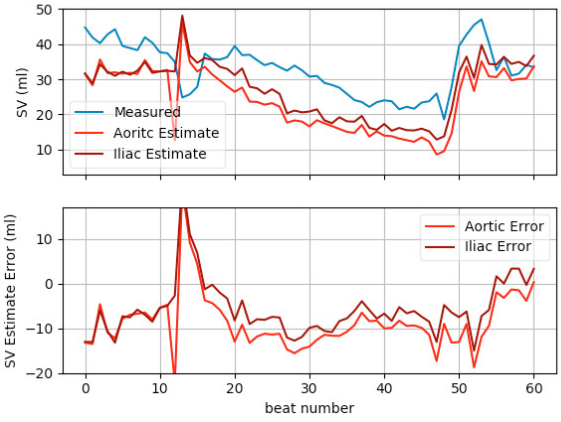
(b) Pig 2 VCO SV measure and estimates.



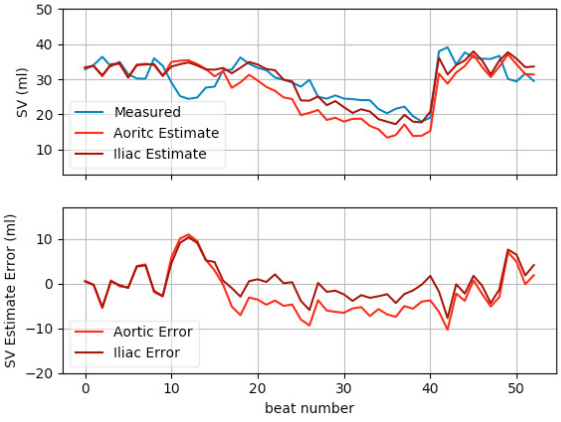
(c) Pig 3 VCO SV measure and estimates.



(d) Pig 4 VCO SV measure and estimates.

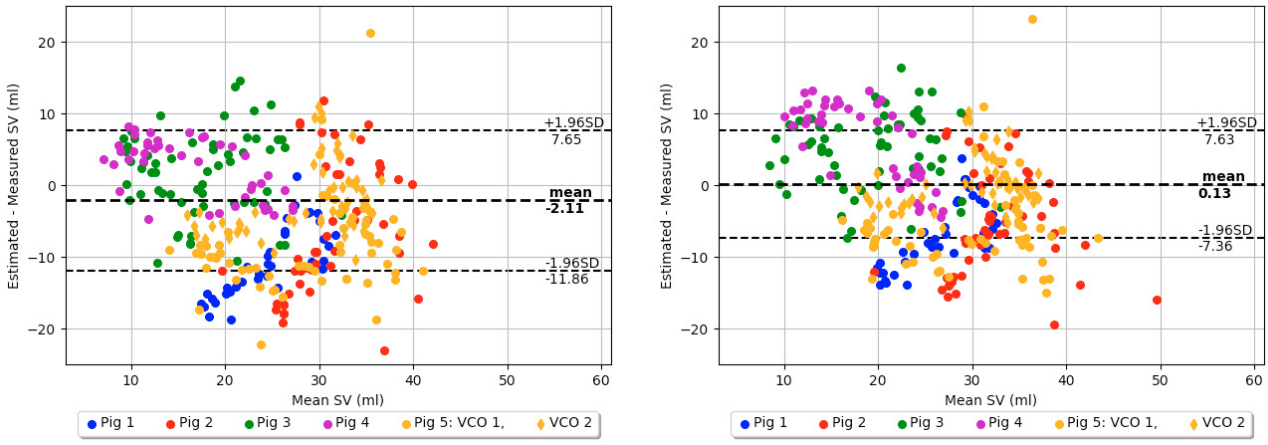


(e) Pig 5 VCO1 SV measure and estimates.



(f) Pig 5 VCO2 SV measure and estimates.

Fig. 2: SV waveforms during VCO: Pigs' 3, 4 and 5 show good SV estimate response. Despite significant reductions in aortic and iliac arterial pressures during the VCO, Pigs' 1 and 2 showed little fall in measured SV. The model still predicts a fall in SV due to the reduction in aortic and iliac pressure during VCO. Note, Figure (b) has a different scale to show the outlier due to an obscure beat near the end of the occlusion.



(a) VCO SV estimate from aortic arch pressure sensor

(b) VCO SV estimate from iliac pressure sensor

Fig. 3: Bland Altman analysis: Bland Altman plots show the degree of agreement between the estimated and measured stroke volume. The mean bias between the measured and estimated systolic times are shown ($\bar{d}$), as well as the limits of agreement ($\bar{d} \pm 1.96 \times SD$) to indicate the expected variation between measure and estimate.

tion and subsequent P_{res} and P_{ex} calculation captures the difference in the *storage* capabilities of the arteries.

For example, assuming the end systole point is accurately found, the parameter product RC, in β of Equation 1, can be identified during diastole for each beat. An accurate PWV measure means the reservoir pressure can be accurately fit to both waveforms, despite the clear difference in their measured signals, as seen in Figure 1 (b). The difference in the reservoir pressure waveform shapes is evident in the assumed arterial properties. Specifically, the aortic pressure waveform has a much higher area under its reservoir pressure signal, due to its high compliance and thus significant expansion and blood storage capability during systole. The iliac pressure, in contrast, has a much larger proportion of excess pressure, suggesting the iliac artery did not expand to the same degree as the aorta, as expected. However, it still captures the same SV estimate. This rational should be generalisable to other arterial sites. Although, it is possible that too distal arteries will not receive a large enough proportion of the ejected SV for a good estimate, particularly during transient behaviour. Hence, further analysis will be required to confirm other arterial sites.

As discussed, estimated SV across all pigs showed consistent response. However, Figures 2 (a) & (b) did not show accurate SV estimates. The consistent response then is in capturing changes in the pressure signals during the VCO, rather than exact measured SV. This issue is one of the current limitations. In a simple system, it is understood that pressure drives flow. Therefore, when changing pressure is input to the model, it responds with changing flow and thus SV. However, the cardiovascular system does not represent quite such a simple system.

In the case of Pigs 1 and 2, it appears the vena cava occlusion led to the expected change in preload and afterload, with the fall in ventricular and aortic end diastolic pressures respectively. However, during this transient state, no significant change in SV appeared, despite the volume signal trending in a similar manner as the pressure waveforms (result not shown). It seems the pigs' cardiovascular system responded by maintaining SV, despite the reduction in ventricular volume, possibly as a function of short to medium term reflex actions, which are known to impact the behavior over the timeframe of a VCO (Sato et al., 1998; Felder and Thames, 1979). It is likely then that if the VCO was maintained for a longer duration, Pigs 1 and 2 would have shown results similar to Pigs 3, 4 and 5, whose cardiovascular systems did not maintain SV.

Despite two of the pigs not demonstrating the desired large change in SV during VCO, it is important to note that the VCO is a external, rapid hemodynamic change. It also occurs on a timescale much shorter than most physiological disease states develop. Thus, in the context of a *worst case* scenario for the model, the results show promise.

4.2 Bland Altman Results

The Bland-Altman plots of Figure 3 clearly show neither arterial pressure site resulted in significantly more bias compared to the other, with mean differences of $\bar{d}_{aorta} = -2.11ml$ verses $\bar{d}_{iliac} = -0.13ml$ respectively. Additionally, the similar widths of each arteries limits of agreement show the SV estimate did not deteriorate by using the distal iliac pressure signal. As expected from Section 4.1, Pigs 1 and 2 are the source of disagreement/error between model and measured stroke volume.

When compared with the Bland-Altman analysis of Kamoi et al. (2017), the results of this analysis support the original findings. In addition, this analysis suggests, even for a *worst case* hemodynamic change, more transient than those presented by Kamoi et al. (2017), the model shows no significant change in SV estimation accuracy. The errors in the analysis may be due to hidden dynamics, such as reflex actions, not currently accounted for in the model. Since there is no *gold standard* continuous SV measure (Wetterslev et al., 2016), it is also possible that the ventricular admittance catheter is an imperfect comparator (Chase et al., 2014).

5. CONCLUSION

Despite two out of five VCOs not causing a significant reduction in SV, the study shows the methods ability to respond quickly to transient hemodynamics. This represents an improvement over the commercially available devices mentioned in the Introduction, which are limited to steady state SV monitoring unless frequent recalibration is performed.

Additionally, the SV estimate based on the iliac pressure signal showed no significant difference compared with the aortic pressure. This is a positive result, as the more arterial sites shown to give accurate SV estimation, the easier the method will be to implement clinically. Future analysis could include using arterial sites with smaller fractions of circulating blood volume, such as the radial arteries, and testing the method on further hemodynamic modifications.

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