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Estimating Central Blood Pressure From a Single Peripheral Pressure Measurement

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Abstract: This paper presents a set of criteria used to identify the parameters describing a tube-load model of the arterial system to estimate central blood pressure *(BP)*. The criteria are generalizable to accommodate for inter- and intra-subject variability encountered in the ICU. The proposed single measurement transfer function *(SMTF)* requires only a single peripheral pressure measurement, commonly available in the ICU, for central pressure estimation, removing the need for an additional measurement of pulse transit time, common to other central BP estimation models. The method was tested using data from six (6) porcine experiments where septic shock was induced and subsequent treatment was performed. Systolic pressure *(SP)*, pulse pressure *(PP)* and root-mean-squared *(RMSE)* errors relative to invasive measurements of aortic pressure were used to assess accuracy. The SMTF method produced mean errors $\leq$5mmHg across all metrics with 84.4, 88.7 and 63.2% of SP, PP, and RMSE, respectively, within this bound of measured central pressure. Peripheral BP accuracy was also assessed as it is commonly used as a surrogate for central BP in clinical settings. Finally, two alternate methods utilizing the same model equations with additional inputs, one using the measured pulse transit time and the other minimizing the RMSE with measured aortic pressure, were implemented to compare the SMTF accuracy to best case outputs given the model equations.

Keywords: Central Blood Pressure, Transfer Function, Wave Reflection, Sepsis, Cardiovascular

1. INTRODUCTION

Arterial blood pressure (BP) monitoring is an important clinical diagnostic tool for directing therapy in patients displaying a wide range of hemodynamic instabilities (Avolio et al. (2009); Kostapanos et al. (2016); Safar and Smulyan (2008)). Clinicians commonly utilise measurements from peripheral arterial sites, predominantly radial or femoral, and infer the state of the cardiovascular system and tailor treatment based on such measurements. However, pulse pressure amplification distorts the poulse as it travels to the periphery resulting in peripheral measurements varying substaintially from central measurements. Clinically, this can lead to misleading targets when applying goal directed treatment (McEniery et al. (2014)). The anatomical proximity of major organs, including the heart, brain and kidneys to central arteries also implies central BP is inherently a more accurate representation of the loads exerted on the organs. Additionally, central BP pulse contains information about the condition of the cardiovascular system crucially relevant to many cardiovascular models (Davidson et al. (2017); Murphy et al. (2019); Pironet et al. (2015)).

Despite wide ranging clinical and academic uses for central BP, direct measurements are uncommon due to the highly invasive, time consuming procedures requiring skilled clinicians. An increased risk of severe infection is also present relative to peripheral measurements. These factors lead to the development of a number transfer functions which combine peripheral BP measurements with mathematical models to estimate central BP. These models range in complexity from generalized transfer functions (GTF), utilizing population based averaged parameters, to adaptive transfer functions (ATF), requiring peripheral BP and pulse transit time (PTT) measurements.

GTF models have been previously validated and shown to be accurate in normal operating conditions. However, the predetermined relation means sudden changes in patient state, from disease or therapy, may not be adequately reflected. Some authors have attempted to increase inter-subject accuracy through additional peripheral BP measurements. Such methods, while accurate, have the oblivious limitation of requiring multiple simultaneous measurements at different peripheral sites. Adaptive models utilise peripheral BP measurements and a single measurement of central-peripheral PTT as model inputs and identify the set of model parameters which best satisfies some constraint. Such models reproduced central BP accurately in a range of experimental conditions (Gao et al. (2016); Swamy et al. (2009)). However, the need for an additional PTT measurement increases complexity (Balmer et al.

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(2018)) and limits the models ability to adapt to complex changes in cardiovascular state, such as those occurring in sepsis, and limits the retrospective use of datasets if such measurements are unavailable. Thus, the need for a fully adaptive single measurement model for accurate central BP estimation in a range of physiological conditions.

This paper presents a novel set of criteria used to estimate central BP by identifying the parameters of a previously validated tube-load model of the arterial system (Swamy et al. (2009); Zhang et al. (2011)). The criteria were selected based on simple physiological assumptions, generalizable to accommodate a variety of patient conditions. The proposed method is compared with three (3) alternate methods for estimating central BP: 1) Invasive femoral pressure measurements; 2) A tube-load model utilizing measured aortic-femoral PTT, denoted $\mathrm{TF}_{Mea,PTT}$; 3) A tube-load model set to minimize the root-mean-squared-error *(RMSE)* of output pressure relative to measured aortic pressure, $\mathrm{TF}_{Min,RMSE}$. All estimates of central BP are compared to invasive aortic pressure measurements. To the authors knowledge there is only one such other attempt and determining a true single measurement method of central pressure estimation (Hahn et al. (2011)), indicating the need for further validation in this area of research.

2. METHOD

2.1 Tube-Load Model

This work uses a tube-load model of the arterial system, representing each path of pulse wave propagation as a uniform, frictionless tube. Each tube is terminated with a frequency dependent impedance load with a pole-zero structure defined:

$$Z_i(\omega) = \frac{Z_{ci}(j\omega + B_i)}{j\omega + A_i} \tag{1}$$

Where ω is the frequency and A_i and B_i are dependent on compliance and resistance of the i^{th} tube and bounded by $0 < A_i < B_i$. Forward propagating waves are reflected at the terminal end of each tube back up the arterial tree and have a magnitude relative to the forward wave multiplied by a reflection coefficient, defined:

$$\Gamma_i(\omega) = \frac{Z_i(\omega) - Z_{ci}}{Z_i(\omega) + Z_{ci}} \tag{2}$$

The pressure at any point along the tube can then be described by the superposition of the forward and backward propagating wave, shifted appropriately by some time constant representing the pulse transit time *(PTT)* from the aorta to peripheral site.

$$P_i(x, jw) = P_{fi}(0, jw)\left[e^{jwPTT_i\frac{x}{d_i}} + \Gamma_i(j\omega)e^{-jwPTT_i\frac{x}{d_i}}\right] \tag{3}$$

Where P_{Fi} is the forward travelling wave, the exponential terms represent the time shift in the frequency domain, x is the distance from the wave origin site to the measurement site and d_i is the tube length. Central and peripheral pressures can then be related by substituting $x = 0$ and $x = di$ into Equation 3, for the proximal and distal tube ends, respectively. This substituting and rearranging gives the peripheral-central pressure transfer function, defined:

$$P_a(\omega) = \frac{e^{jwPTT_i} + e^{-jwPTT_i}}{1 + \Gamma_i(j\omega)}.P_{pi} \tag{4}$$

Where P_{pi} is peripheral pressure and P_a is aortic pressure. Substituting Equation 1 and 2 into Equation 3 gives a relation between central and peripheral pressure for the specified terminal load.

$$\frac{P_a(\omega)}{P_{pi}(\omega)} = \frac{\left(\frac{B_i+A_i}{2} + jw\right)e^{jwPTT_i} + \frac{B_i-A_i}{2}e^{-jwPTT_i}}{B_i + jw} \tag{5}$$

Similar logic is applied to relate arterial entry flow and peripheral pressure. The key difference here is the destructive interference of flow waves opposed to constructive pressure interference. This pressure to flow function is defined:

$$\frac{Q_{ai}(\omega)}{P_{pi}(\omega)} = \frac{\left(\frac{B_i+A_i}{2} + jw\right)e^{jwPTT_i} - \frac{B_i-A_i}{2}e^{-jwPTT_i}}{Z_{ci}\left(B_i + jw\right)} \tag{6}$$

Where Q_{ai} represents the component of central flow entering the i^{th} tube, scaled by some characteristic impedance, Z_{ci}.

2.2 Objective Criteria

Identification of model parameters (A_i, B_i and PTT_i) was achieved by minimizing the errors of four objective criteria derived from simple physiological assumptions about arterial pressure and flow waveforms. This avoids any need to directly assume the shape of the output pressure waves. Errors are calculated for candidate waveforms, referred to herein as P_{can} and Q_{can} for pressure and flow, respectively, and a genetic algorithm is used to find the set of parameters minimizing the sum of the errors. Errors are normalized by their variation over the Pareto optimal set to provide consistent magnitude and avoid domination of one parameter over another.

First, diastolic flow is assumed to be negligible due to aortic valve closure. Q_{can} waveforms are shifted to have the mean diastolic flow at zero flow and the selected model parameters will be the set which minimize the variance of Q_{can} during diastole. Exploitation of zero flow during diatole was effectively used in a previous transfer function to identify model parameters for a given PTT (Swamy et al. (2008)).

Second, candidate flow end-systole $Q_{can}(t_{ES,est})$, defined as the minimum flow for the pulse, can be compared to flow at end-systole estimated from the input arterial pressure, t_{ES}. Additionally, $Q_{can}(t_{ES,est})$ and $Q_{can}(0)$ should be equal due to the aortic valve being closed at both times. The error metric of this criteria then describes the magnitude of the vector between $Q_{can}(t_{ES})$ and the reference intersection of $Q_{can}(0)$ and t_{ES}. Note, $Q_{can}(0)$ is obtained from the diastolic foot of the corresponding pressure wave and t_{ES} found using a weighting function applied to the second derivative of the descending portion of the input pressure wave (Balmer et al. (2020)).

The final two criteria assume the minimum gradient of the selected pressure and flow waves occurs at a time prior to t_{ES}. Ventricular repolarization leads to a rapid decline in ventricular ejection rate prior to the aortic valve closing manifesting as the region of greatest descent on

the pressure and flow pulses (Cheng and Jusof (2018)). Blood inertia causes forward blood flow to continue briefly before the valve fully closes, resulting in a slight offset of this minimum gradient from the dicrotic notch. Accurate identification of this offset from a singular pressure measurement is impractical so a constant offset of $20ms$ prior to t_{ES} is used as a reference for this error criteria.

2.3 Assessment of Results

Relevant standards for assessing accuracy of central BP estimates vary in definitions and predominately refer to the use of non-invasive devices. The Association for the Advancement of Medical Instrumentation ($AAMI$) detail a *"zero-zone"* with estimate BP values within a range of the reference BP are designated a zero-error and values outside the bound are given an error of the difference minus the zero-zone bound. Such definitions are seldom followed in favour of direct comparison error (Kim et al. (2014)). Previous works cite the AAMI standard of 5 ± 8mmHg for accuracy of central BP estimates but perform direct comparisons, presumably as it is more intuitive to interrupt. For consistency, direct comparison of estimate and reference BP, subject to the 5 ± 8mmHg definition of acceptable accuracy, is used in this work. Reference to the consensus document by Stergiou *et. al* are also used to assess error (Stergiou et al. (2018)) While we acknowledge this work uses invasive femoral pressure, due to availability, it is felt that these standards still provide relevant clinical targets.

Each method, including aortic pressure measurements, uses 15sec sections of data to give an average beat for that section. Sections are evenly spaced at two minute intervals throughout the experiment.

3. EXPERIMENTAL DATA

The experimental protocol was approved by the Ethics Committee for use of animals at the University of Liege, Belgium (Reference Number 14-1726). Six (6) pure Pietrain pigs were anaesthetised and mechanically ventilated. Septic shock was induced via a one off infusion of endotoxin (lipopolysaccharide from *E. Coli*, 0.5 mg/kg infused over 30 min). Pre-endotoxin infusion, a 500 mL saline solution is first administered over 30 min to accomatate blood loss in initial surgery. Post-endotoxin additional fluid is given at a rate of 500 mL saline solution over 30 min simulating fluid resuscitation therapy. Aortic pressure in the subjects is continually measured via a catheter with a sampling rate of 250 Hz. P_{lv} and V_{lv} are also continually measured at a rate of 250 Hz via an admittance pressure volume catheter inserted into the left ventricle via an apical stab.

4. RESULTS

Accuracy of the SMTF method was assessed through comparison of systolic *(SP)* and pulse pressures *(PP)* and the root-mean-squared-error *(RMSE)*, relative to invasive measurements of aortic pressure. Two additional tube-load models were also explored to investigate relative accuracy of the SMTF to best case pressure outputs of Equations 5 and 6.

Table 1 shows the mean SP error of each method for all subjects. Relative to peripheral SP, the SMTF produced a reduction in mean error of 50%, yielding a mean error and standard deviation of 2.8 ± 2.2mmHg. Subject 4, highlighted in gray, shows the single exception of peripheral pressure producing a lower error than the SMTF. Potential explanations for this result are offered in Section 5. Mean SP error of the SMTF method was in close agreement with both the $\text{TF}_{Min,RMSE}$ and $\text{TF}_{Mea,PTT}$ methods.

Table 1. Absolute Systolic Pressure Error of Each Method Compared to Invasive Aortic Pressure Measurements: *Mean(Std) [mmHg]*

Subject	SMTF	$\text{TF}_{Min,RMSE}$	$\text{TF}_{Mea,PTT}$	Fem
1	4.2(1.8)	2.9(1.3)	3.7(1.6)	6.3(2.4)
2	3.3(1.9)	2.4(3.9)	1.3(2.8)	4.8(3.2)
3	2.3(1.7)	2.2(1.4)	2.3(1.7)	7.1(3.4)
4	3.0(1.2)	2.3(1.3)	2.8(1.1)	2.8(1.6)
5	1.7(1.7)	1.4(1.4)	2.2(1.9)	5.1(3.2)
6	2.1(1.5)	2.0(2.3)	2.9(1.5)	7.8(2.2)
Mean	**2.8(1.6)**	**2.2(2.0)**	**2.6(1.8)**	**5.6(2.6)**

Table 2 details mean pulse pressure error for each method across all subjects. Significant error reduction of 69.7% is seen between the SMTF and peripheral PP. Relative to measured aortic pressure, the SMTF produced a mean error and standard deviation of 2.6 ± 1.5mmHg. The SMTF method also displayed a reduction in PP error relative to the $\text{TF}_{Mea,PTT}$ method.

Table 2. Absolute Pulse Pressure Error of Each Method Compared to Invasive Aortic Pressure Measurements: *Mean(Std) [mmHg]*

Subject	SMTF	$\text{TF}_{Min,RMSE}$	$\text{TF}_{Mea,PTT}$	Fem
1	2.4(1.5)	1.6(1.3)	1.9(1.5)	11.3(4.2)
2	2.2(1.9)	1.8(4.6)	3.0(3.2)	8.1(3.6)
3	1.9(1.6)	1.6(1.3)	2.1(1.6)	7.3(3.2)
4	1.1(1.0)	1.4(1.3)	1.0(1.0)	5.6(2.5)
5	2.0(1.0)	1.7(1.2)	1.7(1.3)	6.8(4.2)
6	6.4(2.2)	2.8(1.3)	7.3(2.4)	12.7(4.2)
Mean	**2.6(1.5)**	**1.8(2.0)**	**2.8(1.8)**	**8.6(3.7)**

The RMSE of all transfer function methods was relatively consistent across all subjects, with mean errors ranging from 4.2 ± 1.2 for the $\text{TF}_{Min,RMSE}$ method to 4.8 ± 1.1 for the SMTF method. The $\text{TF}_{Min,RMSE}$ method was implemented as a theoretical best case scenario for central pressure estimation using Equation 5 thus, the close agreement of the SMTF implies successful parameter estimation by the criteria.

Table 3. Absolute RMSE of Each Method Compared to Invasive Aortic Pressure Measurements: *Mean(Std) [mmHg]*

Subject	SMTF	$\text{TF}_{Min,RMSE}$	$\text{TF}_{Mea,PTT}$	Fem
1	4.8(1.0)	4.6(1.0)	4.8(1.0)	6.5(1.6)
2	4.5(0.8)	3.8(1.4)	4.2(1.1)	4.9(1.2)
3	4.9(1.3)	4.4(1.0)	4.8(1.1)	5.7(1.0)
4	4.9(0.8)	4.3(0.7)	4.8(0.8)	5.3(0.9)
5	3.5(1.0)	3.1(1.0)	3.7(0.9)	4.2(1.2)
6	6.6(1.8)	5.0(1.9)	5.9(1.8)	7.3(2.1)
Mean	**4.8(1.1)**	**4.2(1.2)**	**4.7(1.1)**	**5.7(1.3)**

Finally, Table 4 details the percentage of data of each method within the specified bounds of ≤ 3, 5 and 10mmHg

relative to invasive aortic pressure measurements. These results are comparable with those presented by Hahn *et. al* in their single measurement estimation of central BP (Hahn et al. (2011))

Table 4. Percent of Total Data Points Falling Within Clinically Relevant Bounds of Accuracy *(%)*

Limit	Metric	SMTF	$TF_{Min,RMSE}$	$TF_{Mea,PTT}$	Fem
≤3	SP	60.7	76.1	72.5	34.2
	PP	71.3	84.8	69.0	12.6
	RMSE	8.1	17.4	3.6	5.9
≤5	SP	84.4	97.2	92.9	50.6
	PP	88.7	98.4	88.1	24.3
	RMSE	63.2	82.8	70.6	41.9
≤10	SP	100.0	99.2	99.6	91.7
	PP	93.8	99.2	99.6	63.2
	RMSE	100.0	100.0	100.0	100.0

5. DISCUSSION

This paper presents a novel, generalizable, selection criteria which is used to identify the parameters of a tube load-model, yielding accurate estimates of central BP, using a single peripheral artery measurement input and nothing else. The method avoids the need of an additional PTT measurement, which is inherently difficult to measure (Balmer et al., 2018). Thus, the criteria provide a non-additionally invasive method for estimating central BP which can account for inter- and intra-subject variability. The method used data from 6 porcine experiments given an initial fluid bolus of 500ml over 30min, followed by an endotoxin injection to induce sepsis and septic shock and further fluid boluses of the same amount to simulate treatment. Additional positive-end-expiratory-pressure (*PEEP*) driven recruitment manoeuvres (*RM's*) were also performed.

5.1 Model Description

The proposed criteria are based on simple physiological assumptions of the arterial flow waveform allowing them to be used in a wide range of patient conditions with similar accuracy detailed in the following:

First, due to the aortic valve being closed, arterial flow during diastole is assumed to be negligible. This assumption has previously been shown to accurately identify model parameters of a tube load model given a direct measurement for PTT (Swamy et al. (2008, 2009)). Model parameters will be such that the variance of the output arterial entry flow during diastole is minimized.

Second, end-systole (t_{ES}) is estimated using the input peripheral pressure waveform by applying a weighting function to the second derivative of the descending slope of the pulse (Balmer et al. (2020)). The weighting function is used to ensure accurate end-systole detection even on dicrotic notch-less pulses. t_{ES} is used to define an error metric describing the difference between end-systole of a candidate model flow wave (Q_{can}) and the intersection of $Q_{can}(0)$ and t_{ES}. Specifically, Q_{can} is a single model flow pulse defined using the feet of the corresponding candidate pressure wave thus, $Q_{can}(0)$ occurs at the start of systole. Again, due to valve closure, flow at $Q_{can}(0)$ and $Q_{can}(t_{ES})$ are equal, meaning $Q_{can}(t_{ES})$ should occur on the intersection of $Q_{can}(0)$ and t_{ES}.

Finally, the maximum negative gradient of the pressure and flow pulses is assumed to occur at some time immediately prior to t_{ES}. Ventricular re-polarization is known to cause the rate of blood ejected from the heart to rapidly decrease which manifests as a region of steepest descent on central pressure and flow waveforms. Due to blood inertia, flow continues briefly after the re-polarization resulting an an offset of the maximum decline in flow rate from the dicrotic notch and t_{ES}. Evaluating this time delay from a single peripheral pressure input is impractical, so a constant $20ms$ delay prior to t_{ES} is used.

5.2 Model Accuracy

Comparison of SMTF SP and PP with reference aortic pressure measurements as well as the relative RMSE gives the absolute errors of the proposed model. Also presented in Section 4 are two additional methods, also utilizing Equations 5-6, intended to investigate the SMTF accuracy compared to best case outputs for the given equations. The $TF_{Mea,PTT}$ method uses the additional input of measured PTT, defined as the difference between aortic and corresponding femoral pressure pulse feet. The $TF_{Min,RMSE}$ used the measured aortic BP to minimize the RMSE between estimated and reference central BP, giving a theoretical best pressure output of the model. Finally, errors relative to invasive peripheral measurements were assessed as any method proposed should be an improvement on current clinical practice. Acceptable tolerable errors of 5 ± 8mmHg are commonly reported when estimating central BP and are used as a reference in this work (Kim et al. (2014); Stergiou et al. (2018)).

The SMTF accurately estimated central SP and PP, resulting in mean absolute errors and standard deviations of 2.8±1.6 and 2.6±1.5mmHg, respectively. These results translate to reductions in mean errors of 50.0% and 69.7% compared with peripheral pressure measurements. The SMTF mean SP errors were well within the acceptable bounds for all subjects and standard deviations ranged from ±1.2-1.9mmHg, indicating high precision. Similar results were achieved for PP estimates, with standard deviation ranging from ±1.0-2.2mmHg, with the exception of Subject 6.

Mean RMSE of the SMTF relative to invasive central BP measurements was 4.8mmHg indicating accurate estimates of complete pressure waveform morphology. Accuracy of waveform morphology, as opposed to select pressure characteristics, was considered important due to the application of central BP in many CVS models. Subject 6 presents the only instance of exceeding the desired level of accuracy, reasons for which are discussed later in this section.

Finally, Table 4 details the percentage of all data within specified bounds of reference central BP. A similar table is requested in the consensus statement for non-invasive BP monitoring (Stergiou et al. (2018)) which requests bounds of ≤5, 10 and 15mmHg. However, a 15mmHg bound resulted in the trivial inclusion of all data points and a reduced 3mmHg bound better described the distribution

of error. Also defined in the consensus statement was a probability of tolerable error ≤10mmHg of 85%. The SMTF method resulted in 100.0, 93.8 and 100.0% of estimates for SP, PP and RMSE within this bound, respectively. In fact, the SMTF SP and PP essentially achieved this probability of tolerable error for ≤5mmHg.

5.3 Comparison of Methods

In addition to direct comparison with invasive aortic pressure measurements, the SMTF method was compared to two alternate transfer function methods utilizing additional, clinically unavailable, information. The $TF_{Mea,PTT}$ used the same model and criteria with the measured central-to-peripheral PTT, removing the need to identify this parameter. Comparison of the SMTF and $TF_{Mea,PTT}$ methods shows the efficacy of implementing the model without PTT. The $TF_{Min,RMSE}$ method used the model equations and minimized the RMSE relative to aortic pressure, giving a best case output given the model equations.

Tables 1-4 show very comparable errors between the SMTF and $TF_{Mea,PTT}$ methods. Mean absolute errors vary by only 0.2mmHg over all metrics with the $TF_{Mea,PTT}$ method producing lower SP error and RMSE and the SMTF lower PP error. Differences in mean absolute errors between the SMTF and $TF_{Min,RMSE}$ methods ranged from 0.6-0.8mmHg. These results indicate the SMTF method is estimating central BP close to optimal for the given equations. Note that, while RMSE was minimized for central BP, the resulting flow wave morphology was not assessed and could be physiologically unreasonable. If flow were accounted for, the error difference between the SMTF and $TF_{Min,RMSE}$ methods may be reduced.

5.4 Sources of Error

The main error source identified was the apparent decoupling between peripheral and central arteries post-endotoxin injection. Previous authors have noted significant changes in SP and PP measurements in experiments involving sepsis and septic shock **?**Carrara et al. (2020). Both studies performed experiments on porcine subjects and reported slight reductions in aortic compliance while peripheral compartments became significantly more compliant. The changes were hypothesized to be due to the differing composition of smooth muscle in peripheral and central arteries and the potential bio-availability of nitric oxide, which stimulates vasodilation, in each section. The changes in vascular tone result in peripheral PP dropping significantly while central PP remained relatively constant, a trend also observed in this work. The drop in peripheral PP was primarily due to a reduction in SP, with diastolic pressure remaining relatively constant, which also caused mean peripheral pressure to drop. Equations 5 and 6 assume mean and diastolic pressures are constant (differing ≥2mmHg) between central and peripheral sites. The final result is a decoupling of the normal pulse wave propagation though the arterial tree, reducing the validity of the underlying model equations in cases of severe septic shock.

In addition to errors induced from severe sepsis and septic shock, Subject 6 presented the only instance of the SMTF method failing to achieve the desired levels of accuracy. A potential explanation for this result is the state of hypovolemia apparent from the start of the experiment, worsening post-endotoxin injection. Atypical dircrotic notches in the aortic pressure measurements and significant differences (≥6mmHg) of diastolic and mean pressures between central and peripheral sites, not present in other subjects, indicate hypovolemia. This is likely as a result of the initial clinical procedures to implement the various measurement devices. which could explain the elevated errors seen in Subject 6. Despite the elevated PP error, the SMTF method still produced a mean reduction in error of 49.6% relative to peripheral PP.

Subject 4 presents the only instance of peripheral pressure producing reduced errors compared with the SMTF in any metric, highlighted in Table 1. An explanation for the decreased peripheral SP error is the significant proportion of this experiment involving PEEP driven RM's. Such manoeuvres have been reported to affect cardiac function in unusual ways causing peripheral SP to drop to, and even fall below, central SP. This may be due to the reduction in cardiac output resulting from the RM (Luecke et al. (2005)). While all subjects received these RM's, Subject 4 received multiple RM's in a short time presumably due to the hemodynamic instability seen and early conclusion of the experiment.

5.5 Limitations

The main limitation of this study is the small sample size. While the use of porcine subjects allowed for accurate and invasive measurements for validation, increased sample sizes and clinical variability is needed to fully validate the SMTF method.

The growing body of research reporting a decoupling of peripheral an central pressures presents a limitation for the application of transfer function models such as the one presented. Potential improvements to these central pressure estimates could be achieved through monitoring bio-markers of septic shock and scaling input pressures accordingly.

The method presented in this work utilized invasive measurements of peripheral pressure to estimate central BP as it was available. Non-invasive methods are currently available for measuring peripheral pressure and while it would be expected using such a device as the input for the SMTF method would increase errors relative to invasive central BP measurements, similar improvements in accuracy over peripheral measurements would be expected.

Finally, as the load used is a generic pole-zero model the resulting parameters α and β have no physiological meaning. While this gives flexibility to the model it could be substituted with a circuit equivalent load to yield physiologically relevant parameters Zhang et al. (2011).

6. CONCLUSIONS

This paper presents a set of criteria to be implemented with a validated tube-load model of the arterial system to accurately estimate central BP from a single peripheral pressure measurement, an nothing else. The model,

denoted the SMTF method, was implemented in six (6) porcine experiments subjected to varying clinical conditions including a baseline fluid boluses, an endotoxin injection to induce sepsis and septic shock, and further fluid boluses to simulate treatment. The SMTF method achieved mean errors and standard deviations of 2.8(1.6), 2.6(1.5) and 4.8(1.1)mmHg for systolic pressure, pulse pressure and root-mean-squared-error, respectively, relative to direct, invasive measurements of aortic pressure.

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