Beat-to-beat estimation of stroke volume to monitor the 
adaptation of the human cardiovascular system in space

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While in-orbit, astronauts are exposed to the extreme conditions of the space environment. Human physiology is majorly affected by microgravity and the most deleterious effects of weightlessness include cardiovascular deconditioning. In an effort to investigate cardiovascular regulation in-orbit, CNES is developing a medical system, Cardiospace, that will be integrated in the future Chinese orbital laboratory TianGong 2 in 2016. The purpose of this study is to contribute to the development of a data post-processing software for the Cardiospace system. Specifically, the present paper elaborates a non-invasive method to estimate important hemodynamic parameters, such as stroke volume, cardiac output and total peripheral resistance. The proposed method uses a three-element model of the blood circulation based on an electrical circuit analogy. The model elements represent aortic characteristic impedance, arterial compliance, and systemic vascular resistance. The performance of the proposed method was assessed and validated during subject clinical trials at the University Hospital of Angers. The model was sucessfully used to examine the evolution of stroke volume during head-up tilt, a procedure during which patients lie on a bed and are tilted at different angles for a defined period of time.

Nomenclature

\[ C_w = \text{arterial compliance} \]
\[ \text{cal} = \text{calibration factor for aortic characteristic impedance computation} \]
\[ HR = \text{heart rate} \]
\[ I = \text{blood flow from the heart} \]
\[ MAP = \text{mean arterial pressure} \]
\[ P = \text{blood pressure in the aorta} \]
\[ P_{\text{diastole}} = \text{diastolic pressure} \]
\[ P_{\text{systole}} = \text{systolic pressure} \]
\[ P_{\text{dicrotic}} = \text{dicrotic notch pressure} \]
\[ PP = \text{pulse pressure} \]
\[ psa = \text{pulsatile systolic area} \]
\[ R_p = \text{total systemic peripheral vascular resistance} \]
\[ t = \text{time} \]
\[ SV = \text{stroke volume} \]
\[ Z_0 = \text{aortic characteristic impedance} \]

Subscripts

\( (\text{ini}) = \text{initial conditions} \)
\( (\text{std}) = \text{standard, “true”} \)
\( (\text{cor}) = \text{corrected} \)
\( (\text{cal}) = \text{calibrated} \)

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I. Introduction

The past 50 years of manned space flights have highlighted our ability to adapt to the hostile conditions associated with the space environment. While in-orbit both the body and mind are challenged by ionizing radiations, isolation and confinement. Additionally, human physiology is affected by weightlessness and by the absence of the gravitational vector, resultant tissue weight bearing and hydrostatic pressure gradient. All these factors have a significant influence on health and functionality of astronauts during missions but also upon return to Earth. Operational considerations are therefore required to develop countermeasures and ensure protection to crewmembers. A better understanding of these factors and their influence is also necessary to optimize crewmembers performance, extend International Space Station (ISS) stays and eventually prepare exploration class missions to Mars.

Since the 1960’s, microgravity-associated physiologic and pathophysiologic changes have been thoroughly examined. Microgravity deleterious effects include among others bone demineralization, muscle atrophy and changes in the balance system. However, the effects of the space environment on the human cardiovascular system attract particular interest. Indeed, returning from a long duration space flight, astronauts experience cardiovascular deconditioning, originating mainly from a shift of blood from the lower extremities to the upper part of the body caused by the absence of gravity. In an effort to investigate cardiovascular regulation on-orbit, CNES is developing a medical system within the framework of a Franco-Chinese convention with the Astronaut Center of China (ACC). This medical system, Cardiospace, will be integrated in the future Chinese orbital laboratory TianGong 2 in 2016.

In this perspective, the primary focus of this study is to contribute to the development of Physiopost, the data post-processing software associated with Cardiospace system. Specifically, the present study aims to propose a non-invasive method for computing important hemodynamic variables such as stroke volume, cardiac output and total peripheral resistance from physiological signals recorded with Cardiospace system. The development of a non-invasive method is a necessity if the data-post processing software is to be used ultimately outside clinical practices or during on-ground post-flight analysis. Stroke volume is the volume of blood, expressed in liters, pumped from the left ventricle of the heart with each beat. Its significance is appreciated clinically for a plethora of medical conditions and patients. It is monitored for instance in surgical and critical care patients. In the realm of sport physiology, assessment of stroke volume is also imperative when evaluating cardiovascular factors that might otherwise limit oxygen transport. Cardiac output is the volume of blood, expressed in [L/min] that the heart pumps in a given unit of time. Eventually, total peripheral resistance is the sum of the resistance of all peripheral vasculature in the systemic circulation, expressed in [mmHg.s/mL]. Cardiac output and total peripheral resistance can easily be derived from stroke volume and therefore only the computation of stroke volume will be mentioned in the following analysis.

This issue is addressed here using a three-element model of the arterial system. This model is used to examine the evolution of stroke volume during head-up tilt, a procedure that attempts to mimic the fluid shift occurring under microgravity conditions. Chapter II presents the three-element model of the arterial system. Chapters III to V expose the steps involved in the computational method elaborated in this study for stroke volume estimation. Chapter VI details the process of the subject clinical trials performed in the University Hospital of Angers to validate the performance of the proposed computational method. Finally, Chapter VII analyses the results of these subject clinical trials.

II. A Three-Element Model Of The Human Arterial System

A plethora of techniques, both invasive and non-invasive are available to measure and monitor stroke volume. The present study focuses on the estimation of stroke volume via the indirect pulse contour analysis method. In the pulse contour analysis method, beat-to-beat stroke volume is computed from a model of the blood circulation based on an electrical circuit analogy. The original concept of the pulse contour analysis method for estimation of beat-to-beat stroke volume was first described by Otto Frank in 1899 as the classic two-element Windkessel model. In 1983, Wesseling et al. developed a pulse contour method based on a three-element Windkessel model. Most pulse contour methods used today are derived from the later model.

Windkessel effect is a term used in medicine to account for the shape of the arterial blood pressure waveform in terms of the interaction between the stroke volume and the compliance of the aorta and large elastic arteries. Windkessel when loosely translated from German to English means “air chamber”, but is generally taken to imply an elastic reservoir.
The aorta is the main vessel distributing blood to the arterial system. It dampens the pulsatile pressure that results from the intermittent outflow from the left ventricle of the heart. The actual dampening is a function of the aortic compliance. Indeed, the walls of the aorta and of the large elastic arteries - e.g. common carotid, subclavian, and pulmonary arteries and their larger branches- contain elastic fibers. Thus, these arteries distend when the blood pressure rises during systole, or cardiac contraction, and recoil when the blood pressure falls during diastole, or cardiac relaxation. The Windkessel effect helps in damping the fluctuation in blood pulse pressure over the cardiac cycle and assists in the maintenance of organ perfusion during cardiac relaxation. The distensibility of the large elastic arteries is therefore analogous to a capacitor while smaller peripheral vessels are analogous to a electrical resistance. Since the rate of blood entering the elastic arteries exceeds that leaving them due to the peripheral resistance, there is a net storage of blood during systole which discharges during diastole. Thus, as vessels start to get smaller the resistance against the blood flow becomes larger.

A. Aortic Characteristic Impedance

The first element in the model is the characteristic impedance of the proximal aorta ($Z_0$). Impedance is a resistance term but applies to situations where flow is discontinuous just like the pulsatile aortic blood flow. $Z_0$ describes the relation between pulsatile flow and pulsatile pressure at the entrance of the aorta. When the left ventricle contracts, blood is ejected into the aorta. As the aorta already contains blood, the existing aortic pressure opposes left ventricular outflow. In reaction to the accelerated blood volume, aortic pressure rises. The rise in pressure will depend on instantaneous flow, cross sectional area of the aorta and aortic compliance. Hence, $Z_0$ represents the aortic opposition to pulsatile inflow from the contracting left ventricle. $Z_0$ has the dimension of pressure divided by flow [mmHg.s/cm$^3$].

B. Arterial Compliance

The second model element is the Windkessel arterial compliance ($C_w$) that describes how much the aortic pressure rises for a certain amount of blood. When a volume of blood is expelled into the aorta, the aorta expands elastically and aortic pressure rises. The increased pressure opposes further inflow into the aorta until left ventricular pressure also rises. A compliant aortic wall expands easily producing only a small rise in aortic pressure, as is the case for the aortic wall of young subjects. Compliance decreases, however, with increasing age. Thus, $C_w$ represents the aortic opposition to an increase in peripheral blood volume. The dimension of compliance is defined as a change in volume dV divided by a change in pressure dP [cm$^3$/mmHg].

C. Total Systemic Peripheral Vascular Resistance

The third element in the model is peripheral vascular resistance ($R_p$). $R_p$ is a measure of the ease of constant blood drainage from the compliant aorta into the peripheral vascular beds. $R_p$ is defined as the ratio of mean pressure to mean flow [mmHg.s/cm$^3$], and is not a major determinant of systolic inflow.

D. The three-element Windkessel Electrical Analog

Figure 1. Three-element Windkessel analog electrical circuit. $Z_0$ characteristic impedance of proximal aorta; $C_w$ Windkessel compliance of the arterial system; $R_p$ total systemic peripheral resistance; $P(t)$ arterial pressure waveform; $P_w(t)$ windkessel pressure; $I(t)$ blood flow from the heart.
In the electrical analog, the arterial compliance $C_a$, is represented as a capacitor with electric charge storage properties. The characteristic impedance of the systemic arterial system $Z_0$ and the total systemic peripheral vascular resistance $R_p$ are represented as energy dissipating resistors. The flow of blood from the heart, $I(t)$, expressed in $[\text{cm}^3/\text{s}]$, is analogous to that of current flowing in the circuit and the blood pressure in the aorta, $P(t)$, expressed in mmHg, is modeled as a time-varying electrical potential. The theoretical modeling as seen in the electrical analog on Fig. 1 is given as:

$$
\left(1 + \frac{Z_0}{R_p}\right)I(t) + C_wZ_0 \frac{dI(t)}{dt} = P(t) + C_w \frac{dP(t)}{dt}
$$

Based on the former electrical analog and similar to Ohm’s law, an analytical expression for stroke volume $SV$ can be formulated as a function of the aortic impedance $Z_0$ and the area under the curve of the systolic blood pressure per beat $psa$, where $SV$ is expressed in millilitres, $psa$ in [mmHg s], and $Z_0$ in [mmHg s ml$^{-1}$].

$$
SV = \frac{psa}{Z_0}
$$

Thus, in order to calculate stroke volume, both the pulsatile systolic area $psa$ and the impedance $Z_0$ must be known or calculated. Computation of the aortic characteristic impedance $Z_0$ is addressed in Chapter III. Computation of the area under the systolic blood pressure curve $psa$ is addressed in Chapter IV.

### III. Computation of Aortic Characteristic Impedance

The crux of the relationship described in equation (2) lies precisely in the ability to determine the aortic impedance $Z_0$. $Z_0$ has indeed been shown to change with age and cardiovascular condition, such as heart rate and blood pressure $^9$. Therefore, even if $Z_0$ is initially assessed by other standard measurement methods, in subjects whose hemodynamic conditions change, such as is the case in orbit, its value must be continuously updated. To date, several pulse contour algorithms based on the electrical analog previously described have been put forth in order to estimate this impedance $Z_0$ (Alderman et al. 1972; Starmer et al. Grat et al. 1992; Tajimi et al. 1983). However, these algorithms had serious limitations or narrow confines of applicability, thereby rendering them impractical $^9$.

Wesseling and co-workers (1983) developed a feasible algorithm where corrections are used for age-dependent, dynamic changes in $Z_0$ due to changes in blood pressure and heart rate, and also for reflections of the pressure waveform from the periphery. For this method, however, calibration against an absolute method of stroke volume measurement (i.e. acetylene, CO2 rebreathing or Doppler ultrasound), performed during preliminary rest experiment, is necessary when absolute values are required. Since then, Antonutto et al. (1995) presented a series of algorithms with the advantage of providing absolute values from stroke volumes integrated into the model. This method does not require any calibration against an absolute method and uses two separate algorithms where the first calculates a resting impedance value from hemodynamic variables without having any other correction factor. The second algorithm then adjusts the impedance as hemodynamic variables change $^9$.

In the present paper, a third hybrid model, combining the strengths of both the Wesseling and Antonutto approaches is proposed. In this hybrid model, the fully contained Antonutto algorithm is first used to provide a absolute initial impedance value from measurable hemodynamic variables such as heart rate, pulse pressure and mean arterial pressure. The absolute initial impedance value obtained from the Antonutto algorithm is then fed into the Wesseling algorithm. The advantage of such an hybrid algorithm is to provide an estimation of absolute and relative values for stroke volume independently from any absolute method of stroke volume measurement. The Wesseling, the Antonutto and the hybrid algorithm developed in this study are presented in sections III.A, III.B and III.C. respectively.

The present paper eventually investigates the performance of each of these algorithms and their ability to monitor stroke volume variations. The three methods were compared against stroke volume measures obtained from a reference data post-processing software, during physiological experiments on two male subjects. The scope of these clinical trials was to validate the proposed hybrid algorithm and subsequently to elect the more appropriate algorithm for Cardiospace data-post processing software Physiopost.
A. The Wesseling Algorithm

The Wesseling algorithm depends on a single approximation of the aortic characteristic impedance, called $Z_{cal}$ in Fig. 2. In this approach, the initial approximation of the impedance $Z_{ini}$ incorporates only the age of the subject as described in Eq. (3), where $a$ and $b$ are constant coefficients.

$$Z_{ini} = \frac{a + age}{b} \quad (3)$$

The value of stroke volume, measured by a standard method, $SV_{std}$, is then utilized to perform the calibration of the initial impedance $Z_{ini}$ and to formulate the final equation used to calculate the calibrated value of stroke volume $SV_{cal}$. Specifically, the calibration factor $cal$ is computed as the ratio of the standard stroke volume $SV_{std}$ to the initial stroke volume $SV_{ini}$. The computation of initial and calibrated stroke volumes, $SV_{ini}$ and $SV_{cal}$, depends on the actual values of the heart rate $HR$ and the mean arterial pressure $MAP$ as described in Eq. (4) and Eq. (5), where $(c-l)$ are constant coefficients.

$$SV_{ini} = \frac{PSA}{Z_{ini}} \cdot \frac{c + d \cdot HR - age(9 \cdot MAP - f)}{g} \quad (4)$$

$$SV_{cal} = \frac{PSA}{Z_{cal}} \cdot \frac{h + i \cdot HR - age(j \cdot MAP - k)}{l} \quad (5)$$

Wesseling et al. derived the model parameters $(a-l)$ through experiments. The values of these coefficients are given in the equations in Fig. 2.

B. The Antonutto Algorithm

The Antonutto algorithm is based on a continuous dynamic recalculation of the aortic characteristic impedance, called $Z_{cor}$ in Fig. 3. In this method, it is first postulated that, during resting conditions, the initial impedance $Z_{ini}$ is related to the initial heart rate $HR_{ini}$, pulse pressure $PP_{ini}$, and mean arterial blood pressure $MAP_{ini}$ as described in Eq. (6), where $(m-q)$ are constant coefficients. As cardiovascular conditions change, Antonutto et al. further postulate that this initial impedance value $Z_{ini}$ can be corrected with the actual values of heart rate $HR$, pulse pressure $PP$, and mean arterial pressure $MAP$ as described in Eq. (7), where $(r-v)$ are constant coefficients. The model coefficients $(m-v)$
given in Eq. (6) and Eq. (7) were determined empirically through experiments.

\[ Z_{\text{int}} = \frac{m}{(n + a \cdot HR_{\text{int}} + p \cdot PP_{\text{int}} + q \cdot MAP_{\text{int}})} \]  

(6)

\[ Z_{\text{cor}} = Z_{\text{int}} \cdot \frac{r}{(s + t \cdot \frac{HR}{HR_{\text{int}}} + u \cdot \frac{PP}{PP_{\text{int}}} + v \cdot \frac{MAP}{MAP_{\text{int}}})} \]  

(7)

C. The Hybrid Algorithm

The hybrid algorithm proposed in the present paper combines the strengths of both the Wesseling and Antonutto approaches. In this hybrid algorithm, the fully contained Antonutto algorithm is first run to provide a standard stroke volume value to calibrate the Wesseling algorithm. This approach allows the calculation of the beat-to-beat stroke volume from an arterial pressure waveform independently from a standard stroke volume measurement method.

D. Derivation of the Cardiac Output and Total Peripheral Resistance

To complete the understanding of cardiovascular adaptation to microgravity conditions, other important hemodynamic parameters can be derived from the pulse contour estimation of stroke volume. The cardiac output \( CO \) can be computed by multiplying the beat-to-beat stroke volume \( SV \) and instantaneous heart rate \( HR \). Finally, the total peripheral resistance \( TPR \) can be derived by dividing the beat-to-beat mean arterial pressure \( MAP \) by the cardiac output \( CO \).

\[ CO = SV \times HR \]  

(8)

\[ TPR = \frac{MAP}{CO} \]  

(9)

IV. Computation Of The Heart Rate, Pulse Pressure And Mean Arterial Pressure Parameters

For each of the three methods presented in Chapter III, the algorithms involve beat-to-beat heart rate, pulse pressure and mean arterial pressure values. These hemodynamic parameters can be obtained for each cardiac beat from the Cardiospace system. The continuous arterial blood pressure signal can indeed be recorded with the Cardiospace system at the finger of the given subject with a dedicated finger cuff device. Beat-to-beat arterial characteristic pressures such as systolic and diastolic pressures can be measured with the Cardiospace system’s BP Holter device.

The pulse pressure \( PP \) is the difference between the systolic and diastolic pressures \( P_{\text{systolic}} \) and \( P_{\text{diastolic}} \) as defined by Eq. (10) and is expressed in mmHg. The systolic pressure \( P_{\text{systolic}} \) reflects the pressure of the heart as it is contracting, whereas the diastolic pressure \( P_{\text{diastolic}} \) reflects the pressure of the heart while at rest.

\[ PP = P_{\text{systolic}} - P_{\text{diastolic}} \]  

(10)

The mean arterial pressure \( MAP \) describes an average blood pressure in an individual. It is defined as the average arterial pressure during a single cardiac cycle and is expressed in mmHg. At normal resting heart rate, \( MAP \) can be approximated by Eq. (11) from the systolic and diastolic pressures. This approximation was used in this study to compute \( MAP \).

\[ MAP = P_{\text{diastole}} + \frac{1}{3}(P_{\text{systole}} - P_{\text{diastole}}) \]  

(11)

Eventually, the heart rate \( HR \) is the number of times the heart beats per minute and is expressed in bpm. In this study, the instantaneous heart rate is measured with Cardiospace system’s ECG electrodes set.

V. Computing The Area Under The Systolic Blood Pressure Curve

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For each of the three pulse contour algorithms presented in Chapter III, the beat-per-beat stroke volume computation calls on the computation of the area \( psa \). The parameter \( psa \), depicted in black on Fig. 4, is defined as the area under the systolic part of the curve above the diastolic pressure. The definition of this area requires the knowledge of the position of the dicrotic notch, the marker for the end of systole. The dicrotic notch is a small downward deflection in the arterial pulse contour immediately following the closure of the heart semilunar valves. It separates the systolic and diastolic phases. For each cardiac beat, four characteristic points can be defined on the arterial pressure waveform. These points are represented on Fig. 4:

- (1) is the end-diastolic point of the previous beat;
- (2) is the systolic peak of the current beat;
- (3) is the dicrotic notch of the current beat;
- (4) is the end-diastolic point of the current beat.

For the purpose of this study, a waveform analysis program was developed to allow the detection of the dicrotic notches on the continuous arterial pressure curve recorded with the Cardiospace system. The detection algorithm presented in the present paper is based on the knowledge of the values and time of the systolic and diastolic points. When this study was started, the detection of these characteristic points was already implemented in the Cardiospace system’s data post-processing software Physiopost.

The dicrotic notch detection algorithm presented in the present paper assumes there should be a dicrotic notch or at least an incisura in the interval set between the systolic peak and the end-diastolic point. For each beat, the dicrotic notch detection procedure monitors the extrema of the waveform and requires the definition of two searching windows. The first searching window is a window in amplitude while the second searching window is a window in time. These searching windows have been defined based on a prior statistical analysis of 20 arterial pressure curve recordings acquired on European astronauts boarding on the ISS. The analysis of these 20 sessions showed that the dicrotic notch pressure occurred between 100 and 320ms after the systolic peak at the latest. Additionally, its amplitude was less than 85% of the systolic peak pressure value. Thus, the dicrotic notch detection algorithm proposed in this study looks for a minimum in pressure simultaneously in:

1) an amplitude window defined as \([0 ; 85\%] * P_{systolic}\)
2) a time window defined as \([t_{systolic} + 100ms ; t_{systolic} + 320ms]\)

The detection algorithm also checks that the detected dicrotic notch has not been located after the end-diastolic point. If this is the case, a tighter detection window is defined and the same detection procedure is repeated.

The difficulty of the detection lies in the fact that the arterial pressure signals recorded with the Cardiospace system are not perfectly smooth. Because of this, many incisuras can be detected. The definition of two detection windows, an amplitude and a time window, allowed to provide a more robust method to overcome this difficulty. On the contrary, the dicrotic notch is in some cases not strongly identifiable. In the case no dicrotic notch is detected, a default dicrotic notch is defined at \( t_{systolic} + 240ms \). The choice of this default dicrotic notch was made after a statistical analysis of the 20 arterial pressure curve recordings acquired on European astronauts boarding on the ISS. This analysis showed that on average dicrotic notches occurred at \( t_{systolic} + 240ms \). The detection algorithm checks that this first default dicrotic notch is not located after the end-diastolic point. If this is the case, a new default dicrotic notch is defined prior to the end-diastolic point.

A display function was added to Physiopost to view detected dicrotic notches and subsequently validate the detection algorithm. The proposed dicrotic notch detection algorithm was validated for the 20 arterial pressure curve recordings acquired on European astronauts boarding on the ISS.

Finally, once all the dicrotic notches have been detected along the entire arterial pressure signal, the beat-to-beat \( psa \) are computed using a trapezoidal method. In the computation of \( psa \) for each given cardiac beat, the start point is the end-diastolic point of the previous beat, whose detection is already implemented in the Physiopost software. The end point is the dicrotic notch of the current beat, detected by the proposed detection algorithm. The discrete values of pressure between the start and the end points are provided by the Physiopost software, which samples the continuous arterial pressure signal recorded with the Cardiospace system at 100Hz.

VI. Subject Clinical Trials

A. Subjects

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The performance of each of the three pulse contour algorithms presented in Chapter III was evaluated at the University Hospital of Angers, using the Cardiospace system. After obtaining informed consent, two male subjects were studied. The subjects were aged 23 and 28 respectively and were in healthy condition.

B. Experimental techniques

In the two patients, the continuous finger arterial pressure signal was recorded using the Cardiospace system’s finger cuff device, a totally noninvasive blood pressure monitor. For each heart beat, the systolic and diastolic pressures were recorded using the Cardiospace system’s BP Holter device. Finally, the heart rate was recorded using Cardiospace system’s ECG electrodes set.

C. Measurement protocols

Two protocols were elaborated and performed separately. Each protocol was carried out on one of the two subjects and were specifically designed to allow the observation of significant changes in arterial blood pressure. In this perspective, postural changes, such as head-up and head down tilts, provide a means of studying the influence of the gravity force upon the cardiovascular system.

When a subject is positioned feet down in the vertical position, he experiences +1g. When tilted horizontally in supine position, the subject experiences a transverse force of 1g. When tilted head down in the vertical position, the subject experiences -1g.

The two protocols designed for this study involved varying degrees of head-up tilt to allow the observation of significant arterial pressure drops. The first objective of these trials is to compare the absolute stroke volume values predicted by each algorithm for each degree of head-up tilt. The second objective is to compare the rates of change predicted by each algorithm between two positions, hence the need for significant pressure drops. For the purpose of these experimentations, the two subjects were attached to a tilt table.

Protocol 1 consisted of two steps:
1) Rest in supine position for 10 minutes
2) Rest in vertical position for 10 minutes

Protocol 2 consisted of four steps:
1) Rest in supine position for 10 minutes
2) Rest in 30° head-up tilt for 3 minutes
3) Rest in 60° head-up tilt for 3 minutes
4) Rest in supine position for 3 minutes

VII. Results

The three pulse contour algorithms, presented in Chapter III, were implemented in the Cardiospace system’s data post-processing software, Physiopost. The arterial pressure waveform and cardiovascular parameters recorded with Cardiospace system on both subjects were retrieved and post-processed with these three algorithms. Additionally, the arterial pressure waveform and cardiovascular parameters were post-processed with the BeatFast software, a commercial software that derives parameters from blood pressure waveforms including stroke volume, total peripheral resistance and cardiac output. In this study, the BeatFast software was used to provide reference stroke volume values. Stroke volume variations predicted by each of the three pulse contour algorithms were thus validated against variations predicted by the BeatFast software.

The simulation of the Wesseling algorithm requires a standard stroke volume value. The mean stroke volume predicted by the BeatFast software during preliminary rest was used as a standard stroke volume value to calibrate the Wesseling algorithm. Figures 5 and 6 show the evolution of stroke volume, during protocol 1 and 2 respectively, predicted by the BeatFast software, the Wesseling, the Antonutto and the hybrid algorithms. The predicted mean stroke volumes and standard deviations (S.D) for each step of protocol 1 and 2 are summarized in Table 1 and 2 respectively. The predicted stroke volume rates of change between successive steps of protocol 1 and 2 are given in Table 3 and 4 respectively.

Figures 5 and 6 show that stroke volumes computed with the three pulse contour algorithms show the visual aspect of the stroke volume curve predicted by the BeatFast software. Tables 1 and 2 show that in absolute values, the Wesseling algorithm predicts closer absolute values to the BeatFast software’s values than the Antonutto algorithm. Additionally, Tables 3 and 4 show that the Wesseling algorithm also predicts consistent rates of change when compared against the BeatFast software’s results. However, the Antonutto algorithm does not provide precise rates of changes when compared against the BeatFast software.
Thus the Wesseling algorithm, which provides close absolute values and rates of change when compared against the BeatFast software, seems to be more valuable for this study than the Antonutto algorithm. However the limit of the previous results is that the standard stroke volume required for the calibration of the Wesseling algorithm was obtained precisely from the BeatFast software’s stroke volumes. Yet, the purpose of this study was to implement an independent data post-processing software that does not require calibration from an external source.

Since the Antonutto algorithm is a fully contained model that does not require calibration and that provides relatively close absolute values when compared against the BeatFast for the initial rest period, this algorithm can be used to calibrate Wesseling algorithm. This is precisely how the hybrid algorithm proposed in this study was elaborated. In the proposed hybrid algorithm, the mean standard stroke volume predicted by the Antonutto algorithm during the 30 first seconds of the each protocol, was computed and and then fed into Wesseling algorithm. The result was conclusive because the hybrid algorithm showed to predict very close rates of change when compared to Wesseling algorithm.

As far as absolute values are concerned, running the hybrid algorithm led to less accurate results than when the Wesseling algorithm was run with a standard stroke volume computed from the BeatFast software. This difference can be explained by the fact that absolute values obtained from the Antonutto algorithm and used for the hybrid algorithm calibration, are slightly superior to the BeatFast software’s absolute values. However, the absolute difference between the hybrid algorithm and the BeatFast software’s results remains low.

Figure 5. Evolution of stroke volume predicted by the BeatFast, the Wesseling, the Antonutto and the hybrid algorithm during protocol 1. (1) the subject is in supine position; (2) the subject is in standing position.

Figure 6. Evolution of stroke volume predicted by the BeatFast, the Wesseling, the Antonutto and the hybrid algorithm during protocol 2 (1) the subject is in supine position; (2) the subject is in 30° HUT; (3) the subject is in 60° HUT; (4) the subject is in supine position.

For protocol 1, there is indeed a 13% absolute difference between the hybrid algorithm and the BeatFast software’s stroke volumes in the period of supine position, while absolute values obtained in the standing position
differ by 8%. As for relative values, rates of change obtained from the hybrid algorithm and the BeatFast software differ by 6%. For protocol 2, there is a 15% absolute difference between the hybrid algorithm and the BeatFast software’s stroke volumes, while absolute values obtained in the 30° and 60° head-up tilt positions differ by 13 and 14% respectively. As for relative values, rates of change obtained from the hybrid algorithm and the BeatFast software between supine and 30°HUT differ by 12%, while rates of change between supine and 60° HUT differ by 8%.

<table>
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<th>Model</th>
<th>Mean ± S.D. (mL)</th>
<th>Mean ± S.D. (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine position</td>
<td>Standing position</td>
</tr>
<tr>
<td>BeatFast software</td>
<td>102.8±7.4</td>
<td>60.5±7.7</td>
</tr>
<tr>
<td>Wesseling</td>
<td>103.8±7.7</td>
<td>58.4±8.1</td>
</tr>
<tr>
<td>Antonutto</td>
<td>112.3±6.4</td>
<td>85.3±10.3</td>
</tr>
<tr>
<td>Hybrid algorithm</td>
<td>116.5±8.5</td>
<td>65.6±10.1</td>
</tr>
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</table>

Table 1. Mean stroke volume ± S.D (mL) predicted by the BeatFast software and the Wesseling, the Antonutto and the proposed hybrid algorithms in supine and standing positions (protocol 1).

<table>
<thead>
<tr>
<th>Model</th>
<th>Mean ± S.D. (mL)</th>
<th>Mean ± S.D. (mL)</th>
<th>Mean ± S.D. (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine position</td>
<td>30° head-up tilt position</td>
<td>60° head-up tilt position</td>
</tr>
<tr>
<td>BeatFast software</td>
<td>92.6±6.0</td>
<td>85.6±8.7</td>
<td>57.5±6.1</td>
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<tr>
<td>Wesseling</td>
<td>92.0±8.5</td>
<td>84.2±9.1</td>
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<td>Antonutto</td>
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<td>76.7±7.8</td>
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<tr>
<td>Hybrid algorithm</td>
<td>106.3±9.8</td>
<td>97.3±10.5</td>
<td>62.4±7.1</td>
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</tbody>
</table>

Table 2. Mean stroke volume ± S.D (mL) predicted by the BeatFast software and the Wesseling, the Antonutto and the proposed hybrid algorithms in supine, 30° and 60° head-up tilt positions (protocol 2).

<table>
<thead>
<tr>
<th>Model</th>
<th>Stroke volume rate of change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine – Standing position</td>
</tr>
<tr>
<td>BeatFast software</td>
<td>-41.2%</td>
</tr>
<tr>
<td>Wesseling</td>
<td>-43.7%</td>
</tr>
<tr>
<td>Antonutto</td>
<td>-23.9%</td>
</tr>
<tr>
<td>Hybrid algorithm</td>
<td>-43.7%</td>
</tr>
</tbody>
</table>

Table 3. Predicted stroke volume rates of change between supine and standing position (protocol 1).

<table>
<thead>
<tr>
<th>Model</th>
<th>Stroke volume rate of change</th>
<th>Stroke volume rate of change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine – 30°head-up tilt</td>
<td>Supine – 30°head-up tilt</td>
</tr>
<tr>
<td>BeatFast software</td>
<td>-7.5%</td>
<td>-38.7%</td>
</tr>
<tr>
<td>Wesseling</td>
<td>-8.4%</td>
<td>-41.2%</td>
</tr>
<tr>
<td>Antonutto</td>
<td>-7.5%</td>
<td>-28.1%</td>
</tr>
<tr>
<td>Hybrid algorithm</td>
<td>-8.5%</td>
<td>-41.3%</td>
</tr>
</tbody>
</table>

Table 4. Predicted stroke volume rates of change between supine and successively 30° and 60° head-up tilt positions (protocol 2).

VIII. Conclusion

The purpose of this study was to develop a non-invasive method to estimate stroke volume variations from an arterial pressure signal recorded with the Cardiospace system. The Wesseling algorithm proved to be more accurate than the Antonutto algorithm when compared against the reference BeatFast software. Indeed, the Antonutto algorithm did not predict correct rates of change. The Wesseling algorithm seemed at first the best solution to
implement in the Physiopost software. However, the use of the Wesseling algorithm is limited by its reliance on a calibrated stroke volume value. The hybrid algorithm proposed in this study copes with this limitation. The proposed hybrid algorithm predicts stroke volume information from arterial pressure independently from an external calibration. Clinical trials showed that the proposed hybrid algorithm predicts correct absolute and relative stroke volume values. The absolute values differ from reference absolute values by less than 15%. The relative values differ from reference relative values by less than 12%. Thus, the three-element model on which this algorithm is based allows a precise computation of stroke volume and subsequently cardiac output and total peripheral resistance. Both the Wesseling and the hybrid algorithm were implemented in the Cardiospace system’s data post-processing software, Physiopost, for delivery to the Astronaut Center of China and to the University Hospital of Angers which are both users of the medical data coming from the exploitation of Cardiospace system. If a higher accuracy is required and a calibrated stroke volume is available from a standard measurement method, the Wesseling algorithm can thus be run to predict stroke volume variations.

IX. Perspectives

The results obtained after processing the physiological signals recorded during clinical trials at the University of Angers were conclusive and allowed the development of a data post-processing software for stroke volume estimation. However, improvements are currently under development to improve the performance of this software. The dicrotic notch detection algorithm proposed in this study can indeed be improved by using a flexible detection window adapted to the length of time of heart beats, instead of a fixed time detection window. This modification is thought to provide a successful dicrotic notch detection for a greater number of heart rate conditions. Eventually, the performance of the proposed hybrid algorithm could be further assessed on a greater number of subjects and on other microgravity platforms such as parabolic flights.

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References


