SEISMOCARDIOGRAPHY: A NOVEL APPLICATION FOR THE NON-INVASIVE ASSESSMENT OF THE FIRST MAXIMAL DERIVATIVE OF LEFT VENTRICULAR PRESSURE

Melonie Burrows[1], Graeme Jahns[1], Geoffrey Houlton[1], Berry van Gelder[2] and Frank Marcus[3]
[1]*Heart Force Medical Inc., Vancouver, British Columbia, Canada*
[2]*Catharina Hospital, Eindhoven, Netherlands*
[3]*The University Medical Centre, Tucson, Arizona, U.S.A.*

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Abstract: Cardiac resynchronization therapy (CRT) results in improved clinical status in patients with heart failure and left ventricular dyssynchrony. One third of CRT patients fail to respond due to the inability to 1) identify non-responders prior to treatment, 2) optimize coronary sinus lead placement for left ventricular pacing and 3) optimize the atrio-ventricular (A-V) and inter-ventricular (V-V) intervals. Although invasive measurements of first maximal derivative of left ventricular pressure (dP/dt_{max}) are used to optimize lead placement and A-V and V-V intervals in CRT, it would be preferable to have a non-invasive assessment of dP/dt_{max}. Echocardiographic dyssynchrony and left ventricular function are current parameters for non-invasively evaluating responders to CRT, but they are not recommended due to their poor reproducibility. We applied recent advances in technology to develop a device called the digital ballistocardiograph (dBG®), which assesses the mechanical function of the heart using triaxial accelerometry. We show that dBG® cardiac events are valid in comparison to 2D transthoracic echocardiography and reliable in comparison to cardiac magnetic resonance imaging. We present preliminary data to support our position that the dBG® could be used as a non-invasive assessment of dP/dt_{max} in heart failure patients to identify responders and optimize CRT.

1 INTRODUCTION

The science of ballistocardiography (BCG) was conceived over a century ago (Starr et al., 1955, Starr et al., 1953) as the study of body motion resulting from myocardial contraction and blood flow from the heart to the periphery (Noordergraff, 1961). During the 1930s to 1960s, there was a surge of studies showing the importance of BCG measurements in clinical cardiology (Starr et al., 1950, Starr and Hildreth, 1952, Starr, 1964), especially in relation to identifying patients with coronary heart disease (Baker, 1950, Scarborough, 1952, Baker, 1968) and development of circulatory abnormalities such as co-arctation of the aorta (Brown et al., 1949, Starr, 1964). Although conceptually attractive, BCG was limited in practice, as the devices were cumbersome requiring fixed installation. In addition, the ability to analyze the signals electronically was not yet available. As such, BCG was impractical to use on a large scale and was abandoned in the 1970s.

Bayevski and colleagues developed seismocardiography (SCG) in 1964. The technique consisted of an accelerometer attached over the sternum area of the chest, which recorded compression waves transmitted through the chest wall from heart contractions during each cardiac cycle. Over the years, SCG has been refined as a technique for cardiac stress monitoring (Jerosch-Herold et al., 1999), left ventricular monitoring during ischemia (Salerno and Zanetti, 1991, Korzeniowska-Kubacka et al., 2005), estimation of left ventricular function (Korzeniowska-Kubacka and Piotrowicz, 2002), and detection of coronary artery disease (Salerno et al., 1991). However, SCG devices were not implemented on a large scale due to the emergence and sudden interest in echocardiography.

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At present, modern accelerometer-based technology is revitalizing the science of BCG and SCG, allowing the motion of the heart to be recorded and analyzed quickly and efficiently for the assessment of cardiac function (Alametsa et al., 2009). We have applied recent advances in hardware and software technologies to develop a new medical device called the digital ballistocardiograph (dBG®), which allows rapid, non-invasive assessment of cardiac events and the force of the heart's contraction, lending itself to patient monitoring and assessment.

Clinical trials have demonstrated that cardiac resynchronization therapy (CRT) results in improved clinical status and lower mortality in selected patients (Abraham et al., 2002, Bristow et al., 2004). However, approximately one third of CRT patients fail to respond due to the inability to accurately 1) identify non-responders prior to treatment, 2) optimize coronary sinus lead placement during the procedure, and 3) optimize the atrio-ventricular (A-V) and inter-ventricular (V-V) intervals (Abraham et al., 2002, van Gelder et al., 2004, Cleland et al., 2005, Jansen et al., 2006). Although invasive measurements of the first maximal derivative of left ventricular pressure (dP/dt_{max}) can be used to increase the number of CRT responders via optimization of lead placement, A-V and V-V intervals, (Kurzidim et al., 2005, van Gelder et al., 2008, van Gelder et al., 2009), it would be preferable to have a non-invasive assessment of dP/dt_{max} (Houthuizen et al., 2011). Echocardiographic dyssynchrony and left ventricular function are current parameters for non-invasively evaluating responders to CRT (Altman et al., 2011, Bai et al., 2011). However, even though echocardiographic variables have been proposed as surrogates for left ventricular dP/dt_{max}, they are not highly recommended due to their poor reproducibility (Thomas et al., 2009). Cardiac timings recorded non-invasively by BCG and SCG have been shown to provide valuable insight into the heart's function (Starr, 1964, Crow, 1994, Lyseggen et al., 2005). As such, if the dBG® could non-invasively predict dP/dt_{max} across a range of heart rates, it would have potential to be a valuable tool for the non-invasive assessment of dP/dt_{max} for identification of CRT responders and optimization of CRT.

In this position paper, we present preliminary data from animal studies to support our position that the dBG® could be used as a non-invasive assessment of dP/dt_{max} in heart failure patients to identify responders and optimize CRT.

2 METHODS

2.1 The Digital Ballistocardiograph®

The dBG® (Heart Force Medical Inc., Vancouver, Canada) consists of three main components: the sensor containing the triaxial accelerometer and two exposed pads for electrocardiograph (ECG) electrodes, the digitizing transceiver unit which conditions and samples the signals and transmits the data to a PC via Bluetooth™, and the software application used for device control and manual data analysis (Figure 1A). The sensor is placed on the sternum in the midline, with its lower edge approximately 3 cm above the xiphoid process (Figure 1B). The triaxial accelerometer (Figure 1C) detects the SCG vibrations generated by the heart's motion. A single, non-diagnostic ECG similar to a lead 1 is also recorded. From specific peaks on the SCG, the following cardiac events can be determined: mitral valve closure (MVC), aortic valve opening (AVO), aortic valve closure (AVC) and mitral valve opening (MVO). Isovolumetric contraction time (IVCT; $t_{MVC} - t_{AVO}$) and isovolumetric relaxation time (IVRT; $t_{AVC} - t_{MVO}$) are derived variables (Figure 2).

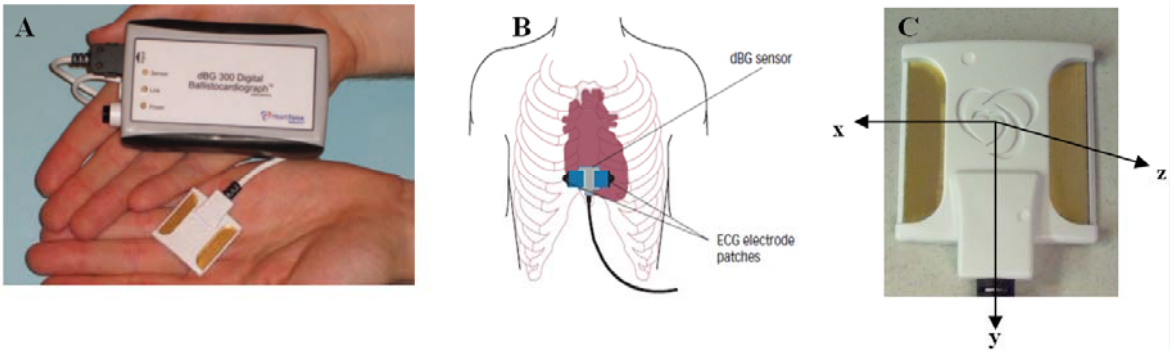

Figure 1: A) The digital ballistocardiograph® sensor and transceiver; B) Digital ballistocardiograph® sensor placement, C) Digital ballistocardiograph® sensor axes from the perspective of the observer; x – from right to left, y – from head to toe, z – from back to chest. Abbreviations: dBG - digital ballistocardiograph; ECG – electrocardiograph.

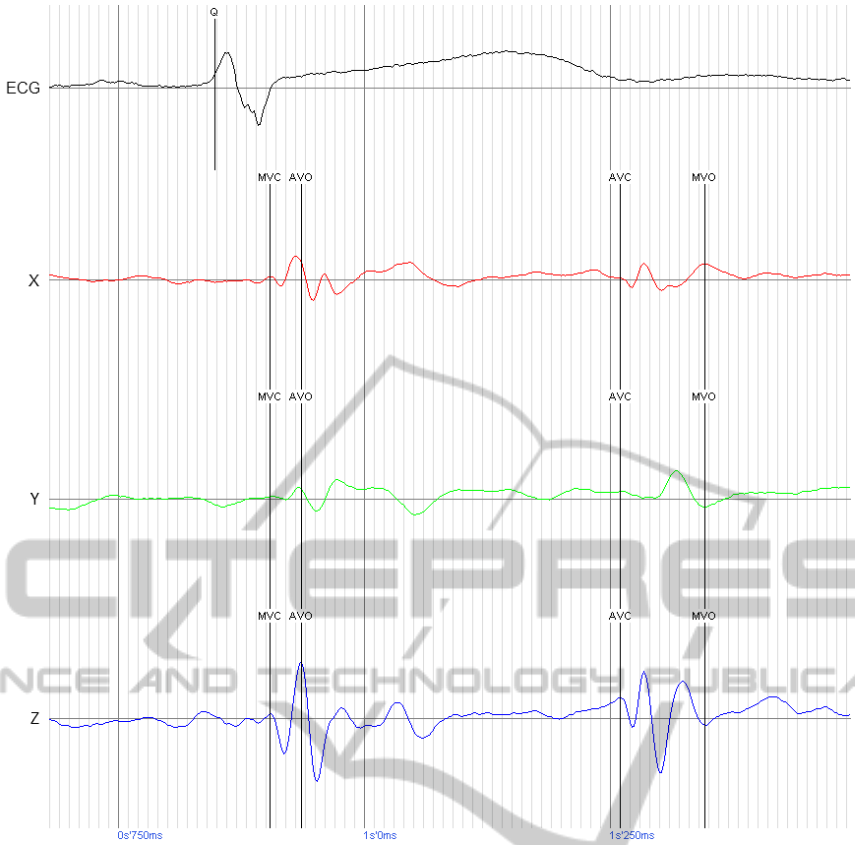

Figure 2: Example digital ballistocardiograph® waveform annotated for four valve timings. Abbreviations: Mitral valve closure – MVC; Aortic valve opening – AVO; Aortic valve closure – AVC; Mitral valve opening – MVO; ECG – Electrocardiogram; X – dBG® sensor axis from right to left, Y – dBG® sensor axis from head to toe, Z – dBG® sensor axis from back to chest.

We investigated the accuracy of cardiac events using the dBG® against the clinical reference standard of 2D transthoracic Doppler echocardiography, and found that the cardiac events measured by dBG® were equivalent to cardiac events measured by 2D echocardiography (95% of dBG® cardiac events fell within ±2SD of echocardiography cardiac events). We have also determined within-device, intra- and inter-operator reliability for the dBG® measurements. Precision was calculated as the root mean square error coefficient of variation (RMSECV, %) and was less than 4% (within), 8% (intra) and 10% (inter) for all cardiac events, which is comparable to the gold standard technique of cardiac magnetic resonance imaging whose reliability is known to be between 2.9–9% (Chuang et al., 2000). As such, dBG® cardiac events are both valid and reliable for clinical use.

2.2 The Digital Ballistocardiograph® in Cardiac Resynchronization Therapy

We used a swine model to investigate if the dBG® variables were predictive of dP/dt_{max} across various heart rate conditions as well as following induced changes in blood volume. We studied 10 hybrid farm pigs (10–16 weeks old), utilizing the dBG® device to measure cardiac timings (MVC, AVO, AVC, MVO), and catheterization to measure left ventricular pressure for computation of dP/dt_{max}.

A guiding catheter (Medtronic, MN, USA) and sensor-tipped PressureWire® (St. Jude Medical Inc., MN, USA) were inserted into the left femoral artery and placed in the apex of the left ventricle under fluoroscopic guidance (HICOR/ACOM-TOP, Siemens, Erlangen, Germany). The PressureWire® was connected to the RadiAnalyser® Xpress (St. Jude Medical Inc., MN, USA) for the measurement of left ventricular pressure. The RadiAnalyser® Xpress

system utilized the PhysioMon™ software (Version 2.02, St. Jude Medical Inc.) for computation of dP/dt_{max}. The output from the RadiAnalyser® Xpress was routed to a signal processing unit (CMS, Module M1006A, Phillips Medical Systems, MA, USA) for simultaneous monitoring of left ventricular pressure. A catheter was inserted into the right femoral artery and placed into the aortic arch under fluoroscopic guidance (HICOR/ACOM-TOP, Siemens). The catheter output was routed to the signal-processing unit (CMS, Module M1006A, Phillips Medical Systems) for simultaneous monitoring of aortic blood pressure. All data output from the CMS were routed to a Biopac MP150 (Biopac Systems Inc., CA, USA). A dBG® proprietary sensor (Heart Force Medical Inc., Vancouver, Canada) was placed on the midline of the sternum with the lower edge of the sensor placed approximately 3 cm above the xiphoid process. A pacing wire (Medtronic) was inserted into the left femoral vein, advanced into the right atrium, and connected to an external, single chamber pacemaker (Medtronic) for pacing of the heart at specific heart rate (HR) conditions. We paced animals via the right atrium for 10 counterbalanced heart rate conditions: 90, 100, 110, 120, 130, 140, 150, 160, 170 and 180 bpm. At each HR, we observed a period of 5 minutes for normalization of hemodynamics, after which we collected all pressure and dBG® data simultaneously for 1 minute. After the pacing protocol was completed, each animal had blood withdrawn equivalent to 10% of body weight, which was subsequently reperfused. After each blood withdrawal/reperfusion, all pressure and dBG® data were collected simultaneously at 1 minute immediately after withdrawal/reperfusion, and 3 minutes after withdrawal/reperfusion.

The left ventricular pressure, dP/dt_{max} and dBG® data collected during the counterbalanced HR conditions were used to assess the relation between dP/dt_{max} and dBG® variables and devise a regression equation to predict dP/dt_{max} non-invasively. The left ventricular pressure, dP/dt_{max} and dBG® data collected during the blood volume conditions were used only to assess if changing blood volumes affected the relation between dP/dt_{max} and dBG® variables. The aortic blood pressure signals were captured only to facilitate time alignment of the dBG® waveforms to the dP/dt waveforms.

We created a proprietary software tool (Heart Force Medical Inc.) to manually annotate the merged data files. We also used the tool to offset the data streams to achieve heart beat synchronization for all data. We manually annotated MVC, AVO, AVC, MVO and a dBG® amplitude measure (dBGv) calculated from the measured cardiac timings on the dBG® waveform, and dP/dt_{max} on the dP/dt waveform. We used a repeated measure regression model to assess if dBGv could predict catheter-based measurement of dP/dt_{max}. Heart rate, HR order and pig weight were used as covariates, and the within pig (between HR and within HR) and between pig variation were assessed. Alpha was set at $P < 0.05$. All statistical analyses were performed by an independent statistician using R (www.r-project.org).

3 RESULTS AND DISCUSSION

dBGv was a significant predictor of dP/dt_{max} ($P < 0.0001$), with a one unit change in dBGv equivalent to 4.01 unit changes in dP/dt_{max} (95% CI 3.00–5.05 units). The relation between dBGv and dP/dt_{max} was consistent across HRs ($P > 0.8$), but varied across pigs ($P < 0.0001$). dBGv remained a significant predictor of dP/dt_{max} ($P < 0.0001$) even when blood volumes were decreasing and increasing.

These preliminary data show a strong predictive capability of dBGv for dP/dt_{max} across heart rates, suggesting that dBGv is a non-invasive surrogate of dP/dt_{max} and is able to detect the force-frequency relation between HR and dP/dt_{max}. The potential of a cardiac amplitude variable to predict dP/dt_{max} has been suggested previously, with peak endocardial acceleration (PEA) amplitude (measured using a micro-accelerometer located on the tip of a transvenous pacing lead), shown to be related to global ventricular contractility independent of recording site and atrial rhythm (Bongiorni et al., 1996). Acute variations in PEA, measured using endocardial leads and implantable device, have also been shown to closely parallel changes in dP/dt_{max} (Rickards et al., 1996).

Despite the remarkable clinical results associated with CRT (Houthuizen et al., 2011), the percentage of non-responders is still 25–35% (Bristow et al., 2004, Cleland et al., 2005). Acute measurements of left ventricular dP/dt_{max} have shown to be necessary to identify non-responders prior to treatment, to optimize coronary sinus lead placement, and to optimize A-V and V-V intervals during CRT to obtain maximal hemodynamic benefit in patients (van Gelder et al., 2004, Jansen et al., 2006, van Gelder et al., 2008, van Gelder et al., 2009). Although catheterization is the gold standard for the assessment of ventricular function, it is invasive, costly and time consuming, and is therefore limited

in its clinical utility. The dBGv measured in this study is a non-invasive surrogate for dP/dt_{max} as it describes the rate of change of contractile force, while being measured from an accelerometer placed on the sternum. During CRT, heart rate is a known variable that, in conjunction with a measured dBGv, could be inserted into an equation to derive a predicted dP/dt_{max} without left ventricular catheterization. An Electrophysiologist could use the predictive equation during CRT to 1) identify patients who experience an increase in dP/dt_{max} at time of coronary sinus lead insertion and therefore likely to be CRT responders, and 2) optimize coronary sinus lead placement and A-V and V-V intervals. The fact that the relation between dP/dt_{max} and dBGv remains strong across changes in blood volume suggests that the predictive relation between dBGv and dP/dt_{max} is robust. The use of the dBG® during CRT could help prevent implantation of CRT devices in the one third of patients who do not currently benefit from this therapy (van Gelder et al., 2004).

4 CONCLUSIONS

In this position paper, we presented a brief history of BCG and SCG and noted that modern technology has revitalized the science of BCG and SCG, allowing the motion of the heart to be recorded, captured and used in the assessment of cardiac function. A new medical device called the dBG® was introduced. The use of the dBG® in CRT optimization was discussed and preliminary data presented showing the strong predictive capability of the dBG® to track dP/dt_{max} across a wide variety of heart rates in swine. The dBG® is small and relatively inexpensive. It appears to have potential to assist in identifying CRT responders and optimizing lead position and A-V and V-V intervals. Clinical studies in heart failure patients are required to document the ability to assist in selecting patients who will benefit from CRT, as well as its use in optimizing A-V and V-V intervals.

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