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Efficacy of Subcutaneous Electrocardiogram Leads for Synchronous Timing During Chronic Counterpulsation Therapy

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Abstract

Counterpulsation devices (CPD) require an accurate, reliable electrocardiogram (ECG) waveform for triggering inflation and deflation. Surface electrodes are for short-term use and transvenous/epicardial leads require invasive implant procedure. A subcutaneous ECG lead configuration was developed as an alternative approach for long-term use with timing mechanical circulatory support (MCS) devices. In this study, efficacy testing was completed by simultaneously recording ECG waveforms from clinical-grade epicardial (control) and subcutaneous (test) leads in chronic ischemic heart failure (IHF) calves implanted with CPD for up to 30 days. Sensitivity and specificity of CPD triggering by R-wave detection was quantified for each lead configuration. The subcutaneous leads provided 98.9% positive predictive value and 98.9% sensitivity compared to the epicardial ECG leads. Lead migration (n=1) and fracture (n=1) were observed in only two of forty implanted leads, without adversely impacting triggering efficacy due to lead redundancy. These findings demonstrate the efficacy of subcutaneous ECG leads for long-term CPD timing and potential use as an alternative method for MCS device timing.

Keywords

counterpulsation; subcutaneous; epicardial; ECG leads; hemodynamics

BACKGROUND

Counterpulsation therapy using intra-aortic balloon pumps (IABP) is the most prevalent form of mechanical circulatory support for HF patients.^{1, 2} Counterpulsation augments myocardial and end-organ perfusion and diminishes ventricular workload, resulting in 43–65% successful clinical outcomes.^{3–6} IABP therapy is cost effective, and device

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implantation through the femoral artery is minimally invasive (modified Seldinger's technique).⁷⁻⁹ IABP inflation and deflation is triggered using surface ECG electrodes, which are suitable for short-term use, are inexpensive, and can be easily replaced. However, IABP therapy cannot be used for long-term support due to the risk of septicemia and limb ischemia due to vascular access and the requirement for patient immobility and supine positioning.^{8, 10, 11}

To provide chronic and ambulatory counterpulsation therapy, several devices including C-Pulse (Sunshine Heart Inc., Eden Prairie MN), CardioVAD (LVAD Technologies, Detroit MI), and Symphony (Abiomed, Danvers MA) are in development or in clinical use.^{12, 13} The C-Pulse is a non-blood contacting cuff that is implanted around the ascending aorta. The CardioVAD is a blood-contacting polyurethane sac that replaces a portion of the descending aorta. The Symphony is a 30-mL sac that is connected to the subclavian artery through a vascular anastomosis and is implanted in a subcutaneous pocket on the right anterior chest.^{14, 15}

Counterpulsation devices require a reliable ECG signal for timing inflation and deflation of balloon or sac¹⁶⁻²³. Synchronous timing for chronic counterpulsation therapy with temporary/surface leads may be a significant clinical challenge¹⁶ due to motion artifact and frequent need to replace surface electrodes. To overcome these limitations, we have developed and tested subcutaneous lead configuration to provide an accurate, reliable ECG signal for chronic counterpulsation therapy.²³

METHODS

Subcutaneous ECG leads

The ECG leads were fabricated by OSCOR (Oscor Inc., Palm Harbor, FL) and the integrated subcutaneous configuration was developed by SCR (SCR Inc., Louisville KY) (Figure 1). The subcutaneous ECG lead configuration consists of four (4) individual leads integrated into a single, electrically isolated cable consisting of four (4) transducers on distal end (ECG sensing) and a single connector on the proximal end that is attached to a signal conditioning and processing module that generates an ECG waveform used to trigger and control counterpulsation timing. Each lead uses a tine for fixation and a 1 cm exposed, non-insulated section for sensing cardiac electric potential. Each of the four sensors is on a 25 cm length lead to provide maximum flexibility and separation distance of up to 50 cm between a pair of sensors. A separation of 15 cm enables detection of a voltage differential (ECG) between paired sensors (Figure 1). A second group of four sensors are used to provide a reliable back-up ECG signal, in the unexpected event of lead migration or fracture in up to two of the four leads in that group. Each group of four sensing leads are packaged into a single silicone coated cable and integrated into a four-pin LEMO male connector (PEI-Genesis), which is mated to a female receptor for ECG signal conditioning and processing. The LEMO connectors have a threaded enclosure as well as an extended end to provide strain-relief.^{16, 22, 23}

Animal Study—All animals used were cared for in accordance with the University of Louisville (UofL) Animal Care Committee and National Institutes of Health guidelines.

Experimental procedures were approved by the UofL Institutional Animal Care and Usage Committee (IACUC).

Chronic Animal Study

Male Jersey calves (n=5, 50–70 kg, Oak Hill Genetics, Ewing, IL) were quarantined for 14 days. Post-quarantine, IHF was induced in animals by selectively injecting 90 micron polystyrene beads into the coronary arteries under fluoroscopic guidance.²⁴ After 45–90 days of IHF induction, clinically comparable IHF were achieved as evidenced by echocardiography (>50% reduction in ejection fraction, left ventricular enlargement, reduction in ventricular wall thickness), EKG (ST segment elevation), and hemodynamic (reduced end organ perfusion, cardiac output, and aortic pressures, higher left ventricular end diastolic pressure and volume) analyses. The IHF animals were prepared for sterile surgery. The calves were endotracheally intubated and maintained under isoflurane anesthesia. A 15 cm incision was made over the 5th rib. The 5th rib was then removed and the aorta was exposed. Heparin was given to maintain an ACT above 250 seconds. The graft was cut to ideal anatomic length. The aorta was partially clamped, an aortotomy was performed, and the CPD graft was anastomosed to the descending aorta using 3–0 polypropylene suture. Hemostasis was confirmed and the graft was de-aired and connected to the CPD. Eight subcutaneous ECG electrodes (two sets of four electrodes) were tunneled in four quadrants surrounding the chest incision and connected to the signal conditioning and processing module externally. Epicardial leads (Medtronic, Minneapolis MN) and subcutaneous ECG leads were implanted and tunneled out next to the driveline. To track migration, surgical staples were used as a placement reference at the location of each subcutaneous ECG lead (Figure 2). A chest tube was inserted and secured for drainage.

After the surgical procedure, the animals were weaned from general anesthesia, transferred to the post-operative care area and monitored continuously for up to 30 days. Subcutaneous and epicardial waveforms were recorded at hourly intervals (30 second epochs). At the end of the study period, the animals were heparinized and euthanized with a bolus of Beuthanasia solution (30 mL I.V.) followed by two boluses of KCl (30mEq). A full necropsy was performed for each subject to qualify the occurrence of internal adverse events and lead migration and fracture. During each necropsy, lead migration, defined as a change in lead position equal to or larger than 1.3 cm from the original location (surgical staple), was visually observed and recorded.

Signal Conditioning and Data Analysis

All ECG data were recorded at 400 Hz (National Instruments, AT-MIO-16E-10, Austin, TX), and were filtered using a clinical standard 60 Hz notch filter (Frequency Devices, Ottawa IL). All waveforms were visualized and recorded using a custom, good laboratory practice (GLP) approved data acquisition system (DAQ). Post-euthanasia, ECG waveforms from the subcutaneous and epicardial leads were analyzed to compare detection rates using a computer program written in MATLAB. Every ECG R-wave landmark for subcutaneous (test) and epicardial (control) waveforms in each data epoch were compared and classified as a true positive, false positive, or false negative using the same algorithm used in the CPD driver. If the QRS complex was detected in both waveforms, the signal was classified as true

positive, and a maximum difference of 150 milliseconds between epicardial and subcutaneous ECG was used to calculate true positive in accordance with ANSI/AAMI EC 57 standard. If the QRS was detected in the epicardial waveform, but not in the subcutaneous waveform it was classified as a false negative. If the QRS was detected in the subcutaneous waveform, but not in the epicardial waveform it was classified as a false positive. These classifications were used to calculate Positive Predictive Value and Sensitivity defined as:

$$\text{Positive Predictive Value (PPV)} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}} \quad (1)$$

$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}} \quad (2)$$

RESULTS

Collectively, the ECG waveforms obtained from the subcutaneous leads during the chronic animal experiments (791 data epochs, 42,772 beats) had a 98.8% PPV and 98.8% sensitivity. Lead migration (n=1) and lead fracture (n=1) were only observed in two out of forty leads implanted in chronic animals. However, lead migration and lead fracture did not adversely impact CPD triggering.

DISCUSSION

This study demonstrated the long-term efficacy of using subcutaneous leads to provide an accurate, reliable ECG waveform for R-wave detection to trigger counterpulsation devices. High sensitivity (98.9%) and PPV (98.9%) values were obtained with the subcutaneous leads in chronic ischemic heart failure animals supported by CPT for up to 30 days. The ECG waveform morphology, fidelity, and R-wave detection were challenged by transient events, such as rapid increases in HR from 50 bpm to over 120 bpm within 3–5 seconds when calves went from laying to standing position and/or potential for significant motion artifact (noise) when calves made rapid movements (ie shaking head, rubbing against stanchions). The small number of false positive and false negative events were not solely due to mismatch with the native myocardial contraction, because if the subcutaneous lead correctly detected an R-wave but the epicardial lead was erroneous, it still registered as a false positive or false negative, reducing PPV and sensitivity values for the subcutaneous leads. Despite these limitations, the performance of the subcutaneous ECG leads exceeded the design criteria of 95% PPV and 95% sensitivity.

Counterpulsation with IABP requires precise timing to ensure that the IABP rapidly deflates prior to ventricular systole to avoid obstructing the aorta, which would have the adverse consequence of increasing ventricular afterload. While CPD timing is more forgiving than IABP because it is not obstructive (fills during ventricular systole), a more stringent ANSI/AAMI EC 57 standard was used to quantify the sensitivity and PPV rates. The trigger source can be adjusted similar to an IABP (fill and empty times) to improve performance and/or

efficacy. False positive may lead to double trigger events, which may augment afterload during systole, and false negatives may lead to missed cycles with reduction in efficacy.

Heart Failure patients may have arrhythmias associated with a pacemaker implant, high voltage T-waves, and large QRS complexes, which may lower the sensitivity and PPQ of the trigger signal obtained from subcutaneous EKG waveform that is used for timing (fill, empty) the CPD. The CPD is contraindicated for HF patients with arrhythmia and, small subclavian artery (< 8 mm), but can be operated using a pacemaker trigger signal. The CPD driver has been validated against the AHA database of EKG waveforms, and the CPD is programmed to go into a 'safe mode' (asynchronous fill-empty cycle) whenever the QRS complex cannot be reliably detected, as previously reported.^{25, 26}

Two of forty prototype subcutaneous leads had a lead fracture or migration, but did not result in the loss of triggering. The CPD was implanted with four subcutaneous ECG leads, but only requires two leads for device timing as the detection algorithm embedded in the CPD driver automatically picks the best ECG signal from any two subcutaneous leads. If a lead fractures or migrates resulting in loss of signal or signal strength, it automatically switches to the other lead pair for ECG signal, providing redundancy.^{27, 28} Once a design freeze has been achieved, clinical-grade subcutaneous leads will complete validation and verification (V&V) testing to demonstrate a lower failure rate comparable or better than with clinically-approved epicardial leads.

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Figure 1.
Photograph of the subcutaneous ECG lead configuration complete with LEMO connector and strain relief (a) with tunneling needle (green arrow) and tine fixation (yellow arrow, b).

Figure 2.

ECG waveforms obtained with epicardial (solid) and subcutaneous (dashed) ECG leads. The performance of the subcutaneous leads was comparable to epicardial leads (98.9% PPV and sensitivity) demonstrating efficacy for counterpulsation timing.