Use Of Paravascular Admittance Waveforms To Monitor Relative Change in Arterial Blood Pressure

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Abstract. Non-invasive methods to monitor ambulatory blood pressure often have limitations that can affect measurement accuracy and patient adherence [1]. Minimally invasive measurement of a relative blood pressure surrogate with an implantable device may provide a useful chronic diagnostic and monitoring tool. We assessed a technique that uses electrocardiogram and paravascular admittance waveform morphology analysis to one, measure a time duration (vascular tone index, VTI in milliseconds) change from the electrocardiogram R-wave to admittance waveform peak and two, measure the admittance waveform minimum, maximum and magnitude as indicators of change in arterial compliance/distensibility or pulse pressure secondary to change in afterload.

Methods: Five anesthetized domestic pigs (32 ± 4.2 kg) were used to study the effects of phenylephrine (1-5 ug/kg/min) on femoral artery pressure and admittance waveform morphology measured with a quadrapolar electrode array catheter placed next to the femoral artery to assess the relative change in arterial compliance due to change in peripheral vascular tone. Results: Statistical difference was observed (p < 0.05) comparing baseline VTI to phenylephrine VTI (246 ± .05 ms to 320 ± .07 ms) and baseline admittance waveform maximum to phenylephrine admittance waveform maximum (0.0148 ± .002 siemens to 0.0151 ± .002 siemens). Conclusion: Chronic minimally invasive admittance measurement techniques that monitor relative change in blood pressure may be suitable for implantable devices to detect progression of cardiovascular disease such as hypertension.

1. Introduction
Noninvasive ambulatory blood pressure monitoring is rapidly expanding as both an instrument in clinical research and a diagnostic tool in clinical practice. However, complications with arm cuff size and arm position relative to the heart often limit the accuracy of ambulatory monitors [1]. Moreover, wearing a blood pressure monitoring device during sleep with cuff inflations programmed to occur at 10-minute or 30-minute intervals causes a reduction of slow-wave (non-REM) sleep and longer nocturnal awakenings [2-4]. External bioimpedance measurements have proved useful for noninvasive monitoring of cardiac hemodynamic parameters, but commercial systems are too cumbersome for ambulatory monitoring [5-7]. Medical device manufacturers have explored the use of implantable pressure transducers to monitor intracardiac pressure but clinical acceptance of these devices have not been promising [8]. Minimally invasive implantable devices may be suitable to monitor pulsatile activity next to an artery that correlates admittance waveform parameters such as maximum, minimum, magnitude and mean values to arterial systolic pressure, diastolic pressure, pulse pressure and mean arterial pressure respectively. The goal of this study was to assess the feasibility of measuring a change in admittance waveform values secondary to change in arterial pressure during an
acute vasoconstrictive drug intervention used to elevate arterial blood pressure. We hypothesize that the change in the admittance waveform measured by an acutely implanted paravascular electrode catheter and external commercially available bioimpedance system are measurable and related to change in systemic arterial blood pressure.

2. Methods

Five domestic female pigs (32 ± 4.2 kg) were anesthetized (propofol, 6mg/kg titrated to effect) and mechanically ventilated at a rate to maintain end tidal CO₂ at 30 to 35 mmHg. Surgical bilateral femoral artery cutdowns were then performed to isolate the femoral arteries. The left femoral artery was surgically dissected leaving the arterial facia intact. A 5F quadrapolar catheter (Pices Quad®, Model 3487-A, Medtronic, Moundsview, MN, USA) was acutely implanted in the arterial facia parallel to the left femoral artery (Figure 1). The right femoral artery was cannulated and a 8F sheath introduced to allow temporary implant of a 7F pressure transducer micro-tipped catheter (Millar Instruments, Houston, TX, USA) to be positioned in the right femoral artery in approximately the same anatomical location as the quadrapolar electrode catheter positioned on the left femoral artery. The left femoral cut down was sutured closed and a 60 minute stabilization period ensued prior to drug intervention. The quadrapolar electrode catheter was connected to an external BIOPAC®, EBI100C bioimpedance amplifier in line with a BIOPAC®, MP150 data acquisition system (BIOPAC Systems, Goleta, CA USA). Femoral artery pressure and electrocardiogram signals were connected to an analog input channel on the MP150 data acquisition system. All signals, impedance magnitude and phase angle, electrocardiogram and femoral artery pressure were recorded at a sample rate of 200 Hz using the AcqKnowledge® software program for Windows (BIOPAC® Systems) and real time conversion of impedance to admittance was displayed on the data acquisition screen. Femoral artery pressure, impedance and admittance signals were processed with a low pass filter at 15 Hz.

**Figure 1.** Anatomic placement of the quadrapolar electrode catheter next to the femoral artery. Current injection (12.5 kHz @ 400 uA sinusoid) was applied between the two outer electrodes (I+ and I-). Voltage sense was measured between the two inner electrodes, polarities corresponding with the applicable current injection electrode (V+ and V-).

A constant rate infusion of phenylephrine (1-5 ug/kg/min) was titrated to effect to elevate and maintain systolic arterial blood pressure ≥ 40 mmHg compared to baseline for a minimum duration of 30 minutes.

3. Analysis

Data was analyzed using the AcqKnowledge® software program over a 30 second duration at baseline and a 30 second duration two minutes after arterial blood pressure stabilized at the aforementioned titrated blood pressure. The following parameters were measured and imported into an Microsoft Excel spreadsheet: R to Y MAX : representing the time interval or Vascular Tone Index (VTI) from the ECG R-wave to the maximum admittance waveform value measured from the paravascular electrode array per cardiac cycle, Y MAX: representing the maximum waveform admittance per cardiac cycle, Y MIN: representing the minimum waveform admittance per cardiac cycle. Arterial systolic and diastolic pressures were also measured during the baseline and drug intervention analysis windows.
Statistical analysis comparing baseline to phenylephrine was performed using a student’s paired T-test with a p-value < 0.05 considered significant.

4. Results
Mean ± standard deviation is shown for Figures 2 & 3. Each graph element represents data combined for all five animals, 30 seconds of data per animal during baseline and 30 seconds of data per animal during the phenylephrine drug intervention.

**Figure 2.** Left: Data depicts and example of an electrocardiogram waveform (red) superimposed on a paravascular admittance waveform (blue). The time duration or vascular tone index (VTI) is shown from the onset of the ECG R-wave to the admittance waveform maximum (Y-Wave Maximum). Right: Data depicts baseline VTI compared to phenylephrine VTI. Statistical difference was observed (p <0.05).

**Figure 3.** Data depicts admittance waveform minimum (Y-Wave Minimum) and maximum (Y-Wave Maximum) comparing baseline to phenylephrine values. Also shown is the corresponding arterial diastolic and systolic pressure during the same time points. In all comparisons shown in this figure, statistical difference was observed (p <0.05).
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