



Multiple Participant Proposal

Performance Assessment of Heart Valves by Non-Invasive Monitoring of Carotid Arterial Waveforms

Total Proposed Costs: \$6,750,000
Number of Participants Sought: 5
Project Cost per Participant: \$1,350,000

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Release Date: June 29, 2020

Closing Date: September 4, 2020
or earlier subject to being fully subscribed

EXECUTIVE SUMMARY

Introduction and Background of KardiaMetrix

KardiaMetrix, based in Nashville, TN was recently established by medical practitioners and biomedical engineers (principally from Vanderbilt University Medical Center) following the discovery of determining a subject's heart stroke volume, performance of their heart valves, the presence of any aortic aneurysm, their blood viscosity, hypertensive state and blood pressure measurement without a cuff, all from non-invasive measurement of their arterial waveforms.

The founders of KardiaMetrix, are the majority owners of VoluMetrix, which is also based in Nashville, TN, and was established in 2015 following the discovery of estimating a subject's blood volume status from invasive and non-invasive venous waveforms. The invasive portion of this technology has been licensed to a major medical equipment manufacturer. KardiaMetrix and VoluMetrix are affiliated companies as per the definitions in the following Contract Documents.

Summary of Proposed Project

KardiaMetrix are soliciting a maximum of five (5) participants to fund an eighteen (18) month study for monitoring heart valve patients from non-invasive carotid waveforms, for a participant cost of \$1,350,000. Forty (40) heart valve failure patients, before and after surgery, are proposed to be monitored at Vanderbilt and Minnesota medical centers, along with twenty (20) healthy subjects. VoluMetrix have IRB and IACUC approvals in place with both institutions and will manage patient monitoring at both institutions.

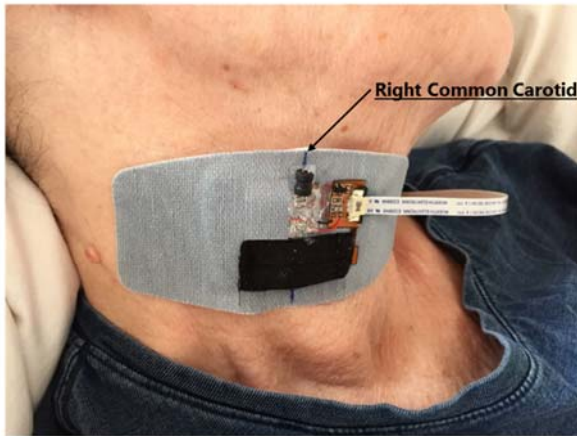
Non-invasive carotid arterial waveforms provide a comprehensive assessment of heart stroke volume, aortic and mitral valve performance, both natural, artificial or surgically repaired. Simultaneous measurement of the carotid arterial waveforms, pulse pressure (PPW), pulse volume change (PVW) and pulse velocity (PUW) are collected by a disposable/recyclable analog wired device, see Figures 1 & 2. These waveforms enable the normalized volumes and energies during each cardiac cycle to be calculated for the subject's heart stroke volume, aortic valve closure, regurgitation, and aortic valve wall compliance. For patients with mitral valve regurgitation, the carotid waveforms can quantify volumes and energies associated with mitral valve regurgitation, and its impact on left ventricle ejected volumes and energies.

Basal septal tissue Doppler velocity trace of a healthy subject is shown in Figure 2a). The ratio of left ventricle ejected volume (LVEV) to aortic valve closure volume (AVCV) is ~ 37 . The non-invasive carotid artery normalized waveforms, PPW and PUW, are shown in Figure 2b) for a 70yr old male, mildly hypertensive. The forward suction wave, due to the aortic valve closing, is clearly defined. Time integration of the PUW waveform yields the normalized LVEV, and time integration of the pulse wavelet velocity (PWU) waveform yields the AVCV and the aortic valve rebound volume (AVBV). The ratio of LVEV to AVCV for the 70yr male shown in Figure 2b) is 37.4. The AVBV is $\sim 30\%$ of the AVCV.

An enhanced analog device will be available for patient studies beginning in November 2020. The current analog wired carotid prototype device will be enhanced throughout the project, and a digital wireless device will be designed and manufactured in limited quantities for 510(k) FDA submission in November 2021.

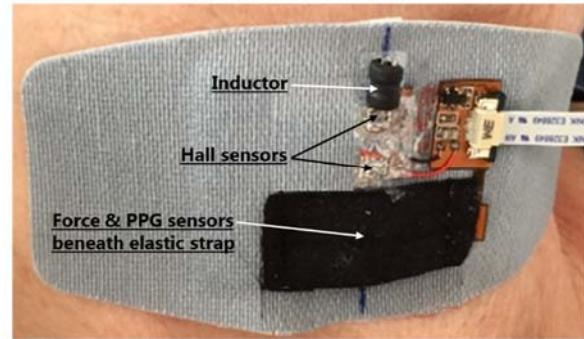
The participants will receive all documented reports throughout the study, have a representative to provide management input into project objectives and deliverables, and attend workshops and technical sessions. The participants will have an option to obtain a royalty free, upgradable license to the waveform executable software for internal use only. The participants will have preferential pricing and access to the final digital wireless non-invasive carotid monitoring device.

74yr female, hypertensive



(a)

Current Prototype Analog Wired Device



(b)

Figure 1. Current Wired Analog Carotid Artery Device, a) over Right Common Carotid Artery, and b) Sensors, Circuit Board, Connector & Ribbon Cable

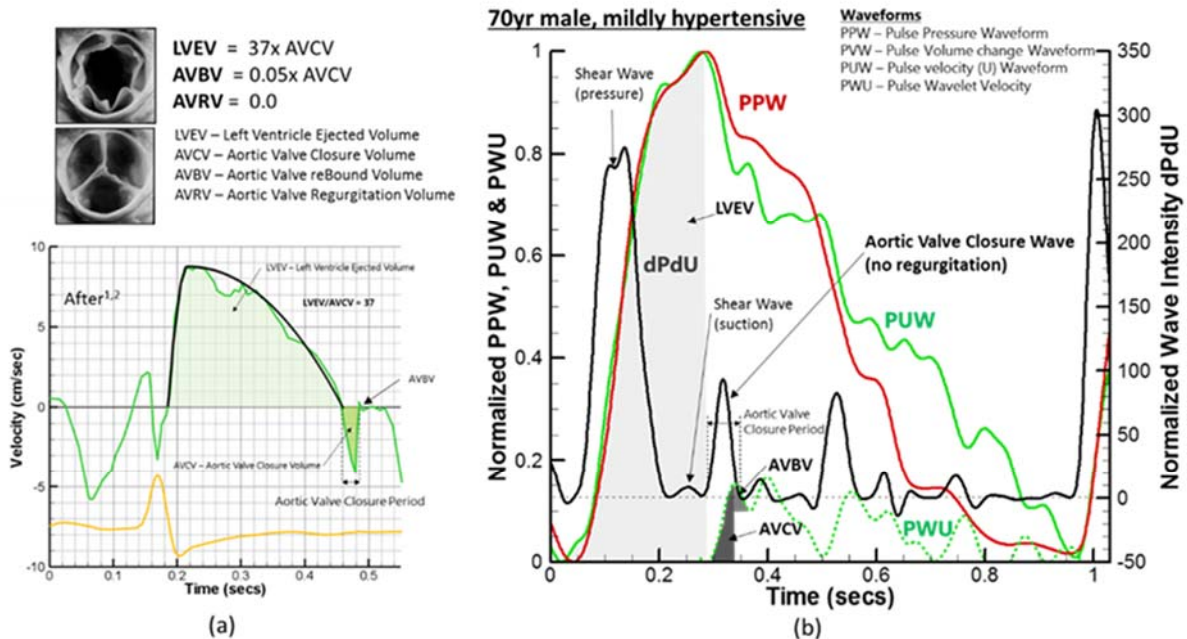


Figure 2. a) Basal Septal Tissue Doppler Velocity Trace of a Healthy Subject, and b) Carotid Arterial Waveforms, Wave Intensity and Wavelet Analyses

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