Development of non-invasive heart failure monitoring for sub-Saharan Africa (SSA)

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Background. Wireless mobile technologies are well-suited to low resource environments where cell phones are available. Avicena LLC is developing non-invasive, rapid cardiac diagnostics using its novel optical sensor/tonometer sensing technology and new mathematical tools applied to the captured waveforms, heart sounds, and ECG. The company is in clinical studies for diagnosis and screening of aortic stenosis [1,2], and has published preliminary studies showing the accuracy of its LVEF [3] and PWV [4] algorithms. The goal of current work is to optimize LVEDP measurement [5], both for commercial development in the U.S. and for deployment in Tanzania. Here we discuss some preliminary studies collected in Tanzania using Avicena's Vivio system, and plans for investigating the potential for Vivio home monitoring of heart failure patients, with a goal to improve patient quality of life and reduce need for hospitalization.

Preliminary data were collected in 2018 using a prototype version of the Vivio that only captures arterial waveforms when held over the carotid pulse. (Current Vivio captures heart sounds as well, and synchronized ECG will be added for the LVEDP study.) Subjects who presented to the visiting physicians of the non-profit Phil Simon Clinic Tanzania Project (Pasadena CA) had blood pressures and Vivio waveforms collected in two locations, urban Arusha and rural Endulen.

Avicena's software collects 'intrinsic frequencies' from waveform data. In engineering terms these measures are angular velocities but in physiologic terms can be considered operating frequencies of the coupled LV + aorta (aortic valve open) and when the AV is closed, the intrinsic frequencies reflect aortic dynamics. IFs are used in turn, with other features, to calculate the cardiac hemodynamic data.

Fig. 1. Intrinsic frequencies of Tanzanian adult subjects differ by urban vs. rural status.

	Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	7.58836	3.50347	2.166	0.0303	*
SamEnt_taw5_m2	11.80410	7.48770	1.576	0.1149	
cD_L3	-28.24051	12.13791	-2.327	0.0200	*
Power_octave_S1_B2	0.32850	0.15665	2.097	0.0360	*
delta_omega_1	-0.04197	0.02352	-1.785	0.0743	.

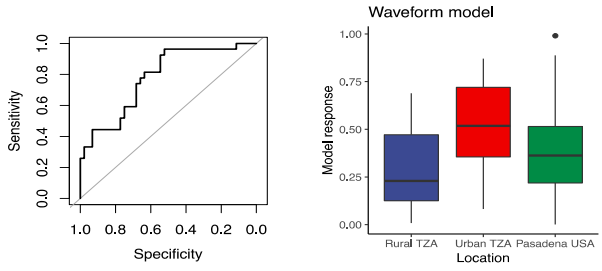

Fig. 1. Multivariable model using only IF and waveform features distinguishes rural from urban Tanzanians (AIC = 0.78, p = 4.4 X 10^{-5}), suggesting specific additional physiologic features that differ significantly between populations. Importantly, none of these features were meaningfully correlated with either central SBP or each other (r<0.3), indicating that *Avicena waveform analysis provides physiologic information about population differences beyond blood pressure*.

Fig. 2. Central blood pressure is higher in urban vs. rural Tanzanians across the lifespan.

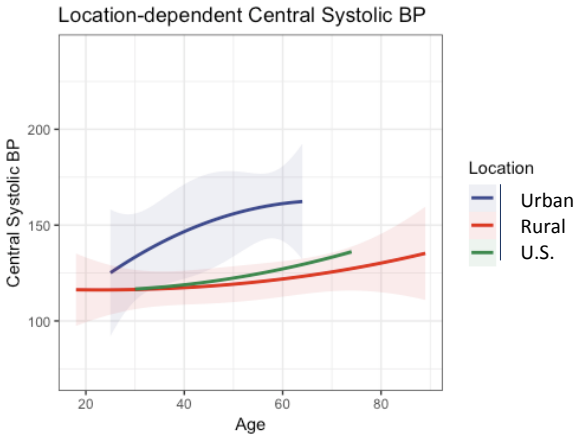

Fig.2. Central SBP was calculated from peripheral BP by a transfer function. After controlling for age and sex, central systolic BP can differentiate urban vs. rural Tanzanians. GREEN: cSBP from the Framingham Study data are superimposed. (Peripheral BP showed a similar pattern, which has been noted by others).

Start of a study in the U.S. to optimize and then validate Vivio LVEDP measurements to those obtained in the cath lab using Millar catheters is anticipated for Q4 2019. Preliminary data supporting this study was obtained in the USC cath labs in Los Angeles [5], was presented to FDA in a pre-submission conference in October 2019. These data will inform the anticipated study planned for Dodoma, with start pending SBIR funding.

Planned Avicena-UDOM HF study. In Phase I (6 mo), UDOM and Avicena UI/UX and app developers will finalize a patient-oriented app (in Swahili). A patient training SOP for the app will be developed and tested on UDOM patients in two hospitals--Dodoma Regional Referral Hospital and Benjamin Mkapa Hospital. In Phase II, subjects will be issued a Vivio system, BP cuff, and scale for daily home use after successfully demonstrating that they (or a caregiver) can capture data using the app. Thirty days of data will be stored on an iPad, with echocardiography done at the start and end of the study (n=240). The hypothesis addressed in the study is that Vivio-LVEDP will rise before return of symptoms or weight gain. Data used in this study will be the supporting data for a following interventional study directed at the hypothesis that daily monitoring of Vivio can be used to reduce hospital admission and improve patient quality of life in UDOM heart failure subjects.

Conclusion. The Vivio system can be used anywhere electricity is available for charging the device, and can be used for real time data transmission if wireless connectivity is available. The long-term goals of this work--beyond noninvasive diagnosis of heart failure--are to identify heart failure deterioration early when interventions are most effective, and ultimately improve the treatment of heart failure in sub-Saharan Africa with a cost-effective, accurate, user-friendly and non-invasive approach.

References

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