New intrinsic frequency measures of cardiac function vs. cardiac MRI as a gold standard

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Background: We recently developed mechanical biomarkers, intrinsic frequencies (ω_1 and ω_2), for functional cardiovascular assessment[1]. Intrinsic frequency (IF) measures are based on mathematical treatment of the left ventricle-arterial system as a coupled dynamic system which is decoupled upon the closure of the aortic valve. IF measures are extracted from a single arterial pressure waveform (e.g. carotid artery waveform) noninvasively. ω_1 and ω_2 provide information about the left ventricular (LV) systolic function and arterial system dynamics respectively[1]. Left ventricular ejection fraction (LVEF) is commonly used to monitor LV systolic function. Here we studied the relationship of EF derived by cardiac MRI (as the gold standard EF measurement) to that derived from ω_1 and ω_2 ($EF=f(\omega_1/\omega_2)$).

Design/Methods: Cardiac MRI was done using an American College of Radiology (ACR) approved GE 1.5 Tesla scanner in Huntington Medical Research Institutes' out-patient facility. Cardiac MRI included 2D fast imaging employing steady state acquisition (FIESTA) sequence in the sagittal, long axis, short axis and radial views. EFs were calculated using short axis slices. All sequences were acquired with ECG gating and breath-holding. The major advantages of IF method is that only the shape of the pressure waveform is required and no calibration is needed. Therefore, we used a regular iPhone camera and flashlight to image the skin motion due to carotid pulse by simply holding, an iPhone 5s over the subjects' carotid pulse. The carotid pressure waves were then extracted from these images using an automatic algorithm (see figure 1 for example waveforms). Intrinsic frequency parameters were calculated from these carotid waveforms. After IRB approval, we studied 11 adult volunteers.

Results and Discussion: Table 1 includes the values of ω_1, ω_2, heart rate (both during the MRI and iPhone measurement), and age for each subject. Table 2 summarizes the EF results from intrinsic frequencies (EF-IF) and from cardiac MRI (EF-MRI). EF-IF and EF-MRI values were calculated blindly by two different investigators. Our results demonstrate strong agreement between the EF-MRI and the EF-IF (computed from noninvasively measured carotid pulse waveform) with average error of 9% and SD of 8%. Our sample size is small and it does not include subjects with low ejection fraction. However, this study is currently active and we are in a process of recruiting more subjects including heart failure patients with reduced ejection fraction (HFrEF) as well as heart failure patients with preserved ejection fraction (EFpEF).

Conclusions: Our results indicate that IF methodology can be used to approximate LVEF. One unique advantage of IF method is that only the shape of the pressure waveform is required. In this regard, IF parameters and consequently, LVEF can be easily derived from non-invasive measurements (e.g. smartphones) and monitored continuously. Future work will use additional MR, echocardiography, and clinical variables to understand the functional implications of IF measurements.

Table 1

Subject No.	1	2	3	4	5	6	7	8	9	10	11
Age	26	54	27	59	29	29	29	42	25	70	30
ω1 (bpm)	105	54.6	98	85.5	99	98	92	86	93	95	88
ω2 (bpm)	42.7	67.5	64	49.5	63	52	40	55	49	39	32
HR-iPhone (bpm)	58	48	66	66	60	59	51	56	60	55	43
HR-MRI (bpm)	60	46	61	85	62	56	57	57	62	55	50

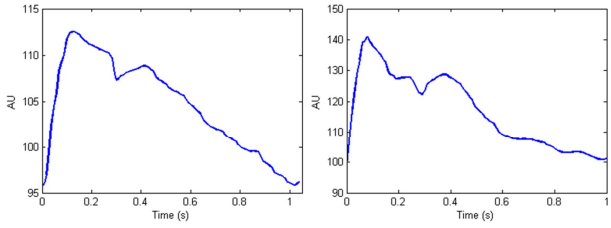

Figure 1: Samples of carotid waveforms from the iPhone

Table 2

Subject No.	1	2	3	4	5	6	7	8	9	10	11
EF_IF (%)	61%	83%	70%	68%	79%	63%	60%	70%	62%	50%	64%
EF_MRI (%)	69%	84%	74%	78%	77%	68%	74%	75%	82%	73%	71%

References: (**1**) Pahlevan NM, Tavallali P, Rinderknecht DG, et al. Intrinsic frequency for a systems approach to haemodynamic waveform analysis with clinical applications. *Journal of The Royal Society Interface.* September 6, 2014 2014;11(98).

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