

# Accuracy of a Novel Handheld Wireless Platform for Detection of Cardiac Dysfunction in Anthracycline-Exposed Survivors of Childhood Cancer



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## Abstract

**Purpose:** Childhood cancer survivors are at risk for anthracycline-related cardiac dysfunction, often developing at a time when they are least engaged in long-term survivorship care. New paradigms in survivorship care and chronic disease screening are needed in this population. We compared the accuracy of a novel handheld mHealth platform (Vivio) as well as echocardiography for assessment of cardiac function [left ventricular ejection fraction (EF)] in childhood cancer survivors with cardiac magnetic resonance (CMR) imaging (reference).

**Experimental Design:** Cross-sectional study design was used. Concurrent evaluation of EF was performed using Vivio, two-dimensional (2D) echocardiography, and CMR. Differences in mean EF (2D echocardiography vs. CMR; Vivio vs. CMR) were compared using Bland–Altman plots. Linear regression was used to evaluate proportional bias.

**Results:** A total of 191 consecutive survivors participated [50.7% female; median time from diagnosis: 15.8 years

(2–44); median anthracycline dose: 225 mg/m<sup>2</sup> (25–642)]. Echocardiography overestimated mean EF by 4.9% ( $P < 0.001$ ); linear regression analysis confirmed a proportional bias, when compared with CMR ( $t = 3.1$ ,  $P < 0.001$ ). There was no difference between mean EF derived from Vivio and from CMR ( $-0.2\%$ ,  $P = 0.68$ ). The detection of cardiac dysfunction via echocardiography was poor when compared with CMR [Echo EF  $< 45\%$  (sensitivity 14.3%), Echo EF  $< 50\%$  (sensitivity 28.6%)]. Sensitivity was substantially better for Vivio-based measurements [EF  $< 45\%$  or EF  $< 50\%$  (sensitivity 85.7%)].

**Conclusions:** This accessible technology has the potential to change the day-to-day practice of clinicians caring for the large number of patients diagnosed with cardiac dysfunction and heart failure each year, allowing real-time monitoring and management of their disease without the lag-time between imaging and interpretation of results. *Clin Cancer Res*; 24(13); 3119–25. ©2018 AACR.

## Introduction

Cardiovascular complications are a leading cause of morbidity and mortality in survivors of childhood cancer (1). These survi-

vors have a greater than 4-fold risk of developing heart failure when compared with age-matched controls (1–3), and there is a strong dose-dependent association between anthracycline exposure and the risk of heart failure (1–3). Outcome following anthracycline-related heart failure is poor; 5-year overall survival is  $< 50\%$  (4, 5), emphasizing the importance of screening for early detection of cardiac dysfunction [abnormal left ventricular ejection fraction (LV EF)] and initiation of pharmacologic therapy prior to the development of clinically overt heart failure. Current long-term follow-up guidelines (6, 7) recommend periodic screening of childhood cancer survivors using an echocardiogram because it is noninvasive and widely available. However, LV EF measured by echocardiography depends on the quality of the acoustic windows which may not be valid in patients with anthracycline-exposed remodeled ventricles (8). Cardiac magnetic resonance (CMR) imaging overcomes these limitations due to its lack of reliance on acoustic windows and the absence of geometric assumption bias (8). However, the applicability of CMR for routine screening is limited, because of significant cost and lack of wide availability. Both these modalities require the patient to be seen in a clinic setting, with the attendant costs and inconvenience due to time away from work/school. Thus, there is

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### Translational Relevance

Cardiovascular complications such as anthracycline-related heart failure (HF) are a leading cause of morbidity and mortality in survivors of childhood cancer. Outcome following HF is poor, emphasizing the importance of early detection of cardiac dysfunction and initiation of pharmacologic therapy prior to the development of clinically overt disease. Unfortunately, the period in time when survivors are at the greatest risk of HF also corresponds to the time when they are least engaged in long-term survivorship care. New paradigms in clinical care and chronic disease screening are needed. The current study describes how a novel handheld mHealth platform (Vivio) can be utilized to accurately screen for cardiac dysfunction in very long-term childhood cancer survivors. Specifically, we found that screening by Vivio was more accurate than standard two-dimensional echocardiography (reference standard: cardiac magnetic resonance imaging), allowing accessible and real-time monitoring of disease without the lag-time between imaging and interpretation of results.

an urgent need to identify accurate as well as accessible screening strategies in these survivors.

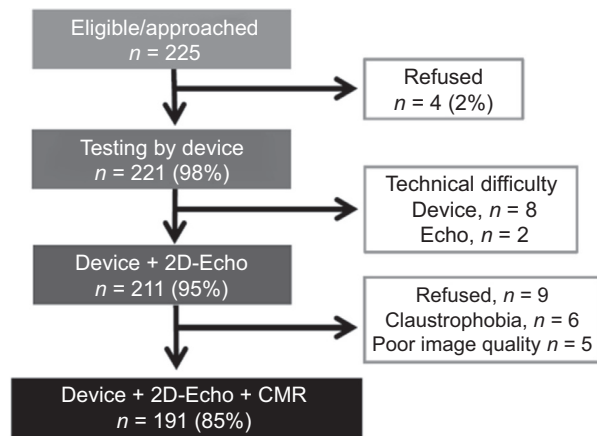
Research has shown that the period in time when childhood cancer survivors are at the greatest risk of cardiovascular complications also corresponds to the time when their level of engagement in comprehensive survivorship care is the lowest (9). Less than 30% of long-term survivors (>5 years from diagnosis) undergo routine risk-based echocardiographic screening (10), but nearly 90% report receiving regular general medical care (10–12), suggesting that long-term survivorship care is largely provided in the primary care setting. Recent advances in mobile technology have facilitated the development of a new sector of healthcare diagnostics (mHealth) that has the potential to combine the utility of echocardiography with the accuracy and validity of CMR, with penetration into the community at relatively low costs (13, 14). Specifically, a recent study demonstrated that a handheld noninvasive wireless device can accurately determine LV EF in nononcology patients with chronic heart failure, providing real-time determination of cardiac function for clinical care (13). The role of such mHealth technology for detection of cardiac dysfunction in at-risk cancer survivors is not known.

The current study compared the utility and accuracy of a handheld wireless device (called the "Vivio" hereafter) as well as echocardiogram (the most widely utilized cardiac dysfunction screening modality in this population) in measuring LV EF in anthracycline-exposed childhood cancer survivors, when compared with CMR (gold standard). Our secondary objective was to examine the association between cumulative anthracycline dose and risk of abnormal LV EF, as measured by the Vivio.

## Materials and Methods

### Study participants

A cross-sectional study design was used. Participants were recruited between November 2014 and May 2017 from the Childhood Cancer Survivorship Clinic at City of Hope (COH). Eligibility criteria included (1) cancer diagnosis before 22 years of age, irrespective of current age; (2) 2 or more years since



**Figure 1.**

Study recruitment and participation flow diagram. Echo, echocardiogram.

completion of cancer treatment; and (3) exposure to anthracycline chemotherapy. Of the 225 survivors who met eligibility criteria, 221 (98%) agreed to participate; all study participants or their parents/legal guardians provided written informed consent; the study was conducted in accordance with the Declaration of Helsinki. The current report is limited to 191 (85%) participants who underwent cardiac evaluation by echocardiogram, CMR, as well as the Vivio (Fig. 1).

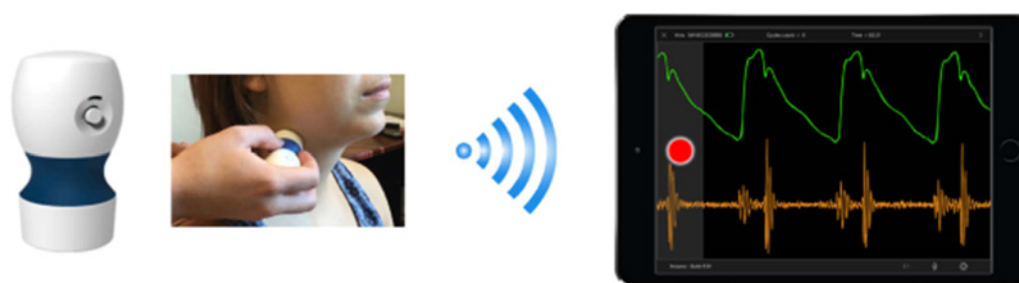
### Cardiac evaluation

Echocardiograms were performed by a designated study technician and consisted of complete two-dimensional (2D) and M-mode, as per the American Society of Echocardiography and the European Association of Cardiovascular Imaging practice guidelines (15). A General Electric Vivid-7 echocardiography machine (General Electric) was used for all study-related echocardiographic evaluations. LV EF was calculated from the apical 4- and 2-chamber views using a modified Simpson's biplane method (16). A deidentified copy of the digitized echocardiogram was sent to the study core cardiology laboratory where LV dimensions, volumes, and EF were measured by a single cardiologist (J. Deterich) who was blinded to clinical and treatment history of study participants.

CMR imaging was performed at COH within 4 weeks of the study echocardiogram using a commercially available GE Twin-Speed system (GE) equipped with parallel imaging methods, electrocardiographic gating, and an 8-channel cardiac phased-array coil. LV volumes and EF were obtained using breath hold ECG-gated 2D cine steady-state free-precession sequences in the 2-, 3-, 4-chamber, and contiguous short-axis orientations. Computation of end-systolic and end-diastolic volumes was performed by trained research personnel (17). Intra- and interobserver (research staff: study cardiologist) correlations were calculated for LV volumes in 40 (~20%) randomly selected study participants; correlation coefficient range was 0.91 to 0.99.

### Vivio-based capture of cardiac function

The Vivio system is a prototype wireless handheld device capable of simultaneous collection of arterial pulse waveform and phonocardiogram data from the carotid artery. Both



**Figure 2.**

Handheld wireless Bluetooth-enabled device (Vivio) with generated carotid waveform that is used to calculate LV EF.

waveforms are streamed wirelessly to any Bluetooth Low Energy (BLE)-compatible device such as an iPad or iPhone (Fig. 2).

On the day of examination, a trained technician placed a wireless sensor (Vivio) on the carotid pulse in order to record the carotid wall displacement waveform. All participants were studied in Fowler's position (sitting up and leaning slightly back). Measurements made from the Vivio were relayed via BLE to an iPad that was designated for research purposes only. The measured waveforms have been shown to be unaffected by the prominence of venous pulsation, obesity, skin color, and neck morphology (13). Recordings were performed on the same day as the echocardiograms, and technicians were blinded to both the echocardiogram and CMR results.

After the waveforms were collected, cardiac cycles were selected by a researcher blinded to study participant clinical history, echocardiography, and MRI data. The selected cycles were used to calculate LV EF via a specialized algorithm called the Intrinsic Frequency (Appendix). In brief, the intrinsic frequency algorithm computes the two dominant dynamic frequencies present within a cardiac cycle before and after the closure of the aortic valve (14). Due to the high nonlinearity of the dynamics of both the LV and arterial systems, a linear regression model was applied to calculate LV EF. Further detail on the methodology for the cycle selection and the calculation of LV EF can be found in the study by Pahlevan and colleagues (13) and is included in the Appendix.

#### Clinical data collection

Baseline data on demographics and cardiovascular risk factors (hypertension, diabetes, and dyslipidemia) were obtained via self-report as well as clinical screening per the Children's Oncology Group long-term follow-up guidelines recommendations (18). Medical records provided the following information: date of diagnosis, type of cancer, cumulative dose of anthracycline exposure, and receipt of chest-directed radiotherapy. Lifetime cumulative anthracycline dose was calculated by multiplying the total dose of each anthracycline (doxorubicin, daunorubicin, epirubicin, idarubicin, and mitoxantrone) by a factor that reflects the cardiotoxic potential of each drug, and then summing the individual doses (7).

#### Statistical analysis

Characteristics of the study population (diagnosis, follow-up duration, and age at follow-up) and treatment-related exposures (lifetime anthracycline dose and chest radiotherapy) were summarized using standard descriptive measures. LV EF was compared across three diagnostic platforms, and Bland-Altman

plots were generated to evaluate agreement between the echocardiography and CMR, Vivio and CMR, and echocardiography and Vivio; 1-sample *t* test was performed to examine whether the mean difference between screening approaches was greater than 0; linear regression analysis was performed to examine for proportional bias. Pearson correlation coefficients were calculated between LV EF obtained from the Vivio, echo, and CMR. Sensitivity, specificity, false-negative rate, and false-positive rates were calculated to assess the accuracy of the Vivio as well as echocardiography for detection of abnormal LV EF as measured by CMR (gold standard). The cutoff for abnormal (LV EF < 45% by CMR) was per established thresholds in oncology (19–21) and nononcology populations (22–24), as it is a clear indicator for referral to a cardiologist for clinical assessment. Multivariable logistic regression analysis was performed to examine the risk of abnormal LV EF (<45%), as measured by the Vivio, according to cumulative anthracycline dose (<250 mg/m<sup>2</sup>, ≥250 mg/m<sup>2</sup>) and adjusted for clinically relevant covariates [age at diagnosis, sex, time since completion of therapy, chest radiotherapy exposure (any), body mass index (BMI), and cardiovascular risk factors (hypertension, diabetes, and dyslipidemia)].

## Results

Median age at evaluation was 25.7 years (range, 13–60 years; Table 1), and survivors were a median of 15.8 years (range, 2–44 years) from completion of cancer treatment. The prevalence of hypertension, diabetes, dyslipidemia, and obesity (BMI ≥ 30) was 13.1%, 7.3%, 10.5%, and 18.8%, respectively. Median cumulative anthracycline dose was 240 mg/m<sup>2</sup> (range, 25–642 mg/m<sup>2</sup>), and 11% had received chest-directed radiotherapy. Acute lymphoblastic leukemia [*N* = 77 (40.3%)] and Hodgkin lymphoma [*N* = 31 (16.2%)] were the most common diagnoses. The prevalence of abnormal LV EF (<45%) was 10.5% (*N* = 20; Vivio), 2.1% (*N* = 4; echocardiography), and 3.7% (*N* = 7; CMR); the prevalence was higher when a cutoff <50% was used across platforms (19.4%, Vivio; 6.3% echocardiography; 9.4% CMR).

The mean EF by the Vivio (56.5%) did not differ substantially from that by CMR (56.8%). The mean EF (61.7%) by echocardiography was greater than that measured by CMR. Bland-Altman plots confirmed a low mean difference between the Vivio and CMR [−0.24%, *P* = 0.68; Bland-Altman limits of Agreement (±1.96 SD), −15.63% to 15.15%; Fig. 3A] and high mean difference between echocardiography and CMR (4.93%, *P* < 0.001; −11.47% to 21.33%; Fig. 3B); the mean difference between echocardiography and the Vivio was comparable with that seen

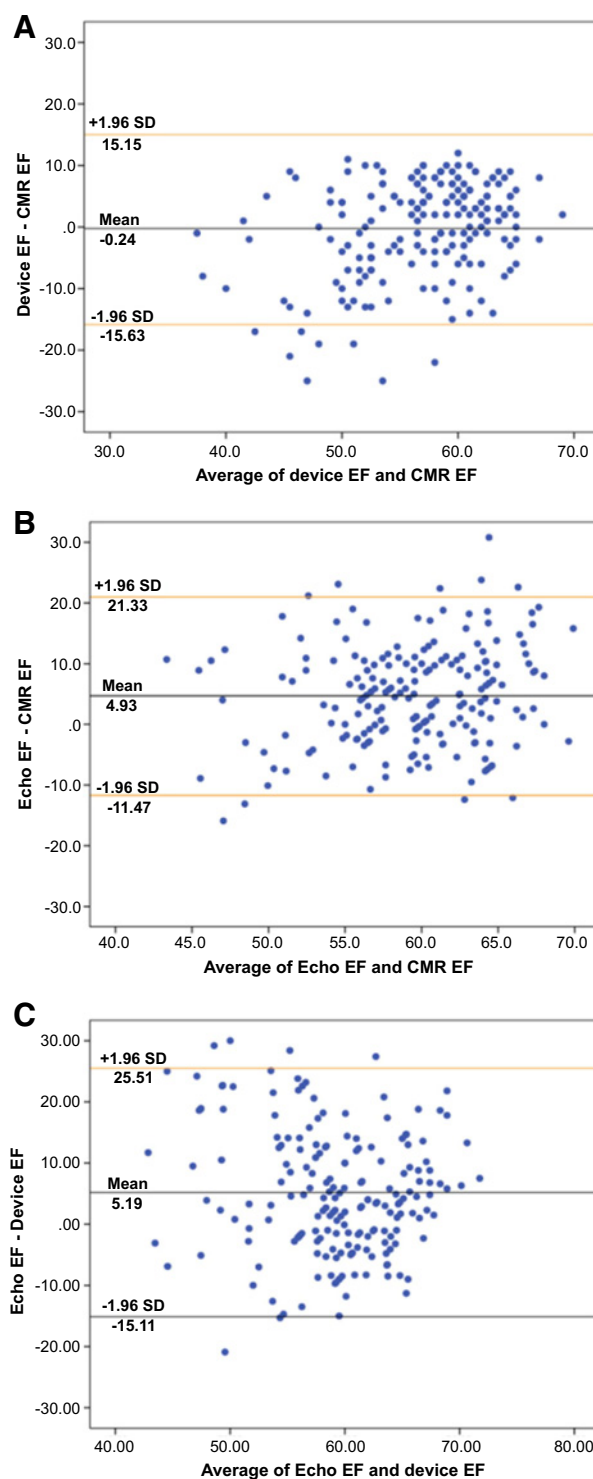
**Table 1.** Demographic and treatment characteristics

Characteristics	Participants (N = 191)
Sex, N (%)	
Male	97 (50.7)
Female	94 (49.3)
Race/ethnicity, N (%)	
Non-Hispanic white	77 (40.3)
Hispanic	103 (53.9)
Other	11 (5.8)
Age at examination, years	
Median, range	26.6 (6.7–55.8)
Age at diagnosis, years	
Median, range	11.5 (0.4–22)
Time since diagnosis, years	
Median, range	15.8 (2–44)
Diagnosis, N (%)	
Hematologic malignancy	152 (79.6)
Acute lymphoblastic leukemia	77 (40.3)
Acute myeloid leukemia	24 (12.6)
Hodgkin lymphoma	31 (16.2)
Non-Hodgkin lymphoma	20 (10.5)
Solid tumor	39 (20.4)
Osteosarcoma	12 (6.3)
Ewing sarcoma	11 (5.7)
Other	16 (8.4)
Lifetime anthracycline, mg/m <sup>2</sup>	
Median, range	240 (25–642)
<100 mg/m <sup>2</sup>	21 (11.0)
100–199 mg/m <sup>2</sup>	54 (28.3)
200–299 mg/m <sup>2</sup>	49 (25.7)
300–399 mg/m <sup>2</sup>	42 (22.0)
≥400 mg/m <sup>2</sup>	25 (13.1)
Chest radiotherapy, N (%)	
Any	21 (11.0)
Cardiovascular risk factors, N (%)	
Hypertension	25 (13.1)
Diabetes	14 (7.4)
Dyslipidemia	20 (10.5)
Obese (BMI ≥ 30/kg/m <sup>2</sup> )	36 (18.8)

with CMR (5.19%,  $P < 0.01$ ;  $-15.11\%$  to  $25.51\%$ ; Fig. 3C). Linear regression analysis demonstrated a proportional bias for both the Vivio ( $t = 4.8$ ,  $P < 0.001$ ) and echocardiography-based ( $t = 3.1$ ,  $P < 0.001$ ) measurements when compared with CMR. The correlation was strongest between the Vivio and CMR ( $R = 0.44$ ,  $P < 0.001$ ) and weakest between the Vivio and echocardiography ( $R = 0.12$ ,  $P = 0.10$ ).

Compared with CMR-determined cutoff of  $<45\%$  for LV EF, echocardiography demonstrated low sensitivity (14.3% to 28.6%) and high false-negative rates (71.4% to 85.7%) regardless of echocardiogram-based cutoff for abnormal ( $<45\%$  or  $<50\%$ ; Table 2). On the other hand, there was high sensitivity (85.7%) and a low false-negative rate (14.3%), irrespective of Vivio-based cutoffs for abnormal (Table 2). The small numbers of participants with LV EF  $<45\%$  by CMR precluded detailed characterization of participants with false-negative or -positive results.

There was a dose-dependent increase in the prevalence of cardiac dysfunction (LV EF  $<45\%$ ), as measured by the Vivio and anthracycline dose:  $<100$  mg/m<sup>2</sup> (4.8%), 100–199 mg/m<sup>2</sup> (9.1%), 200–299 mg/m<sup>2</sup> (19.8%), 300–399 mg/m<sup>2</sup> (23.8%),  $\geq 400$  mg/m<sup>2</sup> (36.0%). Overall, there was a 4.7-fold (OR = 4.7; 95% confidence interval, 1.2–10.8) increased risk of Vivio-measured cardiac dysfunction in survivors treated with high-dose ( $\geq 250$  mg/m<sup>2</sup>) anthracycline compared with those treated with lower ( $<250$  mg/m<sup>2</sup>) doses.



**Figure 3.** Bland-Altman plots for agreement of (A) CMR imaging with Vivio (Device), (B) 2D echocardiography (echo) and CMR, and (C) echo and Vivio.

## Discussion

The principal findings from the current study were that a handheld wireless carotid waveform-based measurement of

**Table 2.** Screening accuracy of Vivio and echocardiogram compared with CMR for detection of LV EF <45%<sup>a</sup>

Variable, N	Vivio (<45%)	Vivio (<50%)	2D Echocardiogram (<45%)	2D Echocardiogram (<50%)
Participants with abnormal LV EF, N (%)	20 (10.5)	37 (19.4)	4 (2.1)	12 (6.3)
Sensitivity	85.7%	85.7%	14.3%	28.6%
Specificity	92.4%	83.2%	98.3%	94.6%
False-negative rate	14.3%	14.3%	85.7%	71.4%
False-positive rate	7.6%	16.8%	1.7%	5.4%

<sup>a</sup>Of note, 7 (3.7%) participants had LV EF <45% by CMR.

LV EF was accurate and had a low false-negative rate when compared with CMR in childhood cancer survivors treated with anthracyclines. Testing by the Vivio was feasible, with >95% of readings having adequate data points for LV EF measurement. We also confirmed the poor diagnostic yield of 2D echocardiography when compared with CMR, with corresponding low sensitivity and high false-negative rates. There was a dose-dependent increase in the risk of cardiac dysfunction and anthracyclines, as measured by the Vivio, supporting the well-established relationship between anthracycline dose and risk of cardiac dysfunction in childhood cancer survivors. The information from the current study can be used in the development of new paradigms in survivorship care delivery in at-risk cancer survivors, and for the implementation of interventions with real-time monitoring of efficacy in survivors with cardiac dysfunction.

It is important to note that the vast majority of childhood cancer survivors living in the United States are still relatively young (70% are <40 years of age; ref. 25), comprised of a technology-engaged population willing to consider health-promotion programs to maintain their well-being. Further, these young adults may no longer live near their treating institutions (9, 10, 12), emphasizing the need for flexible mHealth platforms to deliver sustainable survivorship care for these survivors, regardless of location. The current study represents the first step toward building a comprehensive mHealth platform, namely the need to establish the accuracy of mobile technologies against existing approaches to cardiac screening.

CMR is considered the reference standard to which alternative cardiac imaging approaches are compared for measurement of cardiac function (22, 26, 27). Armstrong and colleagues (28) were among the first to examine the utility of screening by CMR versus echocardiography in 114 adult survivors of childhood cancer survivors. Using a cross-sectional study design, they found a low sensitivity (25%) and high false-negative (75%) rate of 2D echocardiography (biplane method) when compared with CMR (28). The current study includes the largest number of childhood cancer survivors known to have undergone simultaneous screening by CMR and echocardiography, and confirms the low sensitivity and high false-negative rate of 2D echocardiography when compared with CMR. Importantly, in both studies, LV EF as measured by 2D echocardiography was on average 5% higher than that measured by CMR, providing further confirmation that LV EF measurements obtained from these two modalities are not comparable. For the current study, abnormal LV EF was defined as <45%, which is an established CMR-based threshold in oncology (19–21) and nononcology populations (22–24). Per our data, a CMR-based threshold of LV EF <45% would also correspond to an echocardiogram-based measurement of LV EF <50%, a cutoff used to define LV systolic dysfunction per the common terminology of adverse events (CTCAE version 4;  $\geq$  grade 2 toxicity).

When performing population-based screening for asymptomatic disease, it is generally preferable to implement a sequential

screening strategy, relying on a less expensive and less invasive test first, followed by a more expensive and invasive test which may have greater sensitivity and specificity (29, 30). In this context, there is inevitably a net loss in sensitivity, because only a proportion of the individuals who tested positive on the first test are brought back for additional testing. Therefore, it is important that the first screening test has a high sensitivity, regardless of thresholds used to define abnormal, as was the case in the current study (sensitivity of the Vivio: 85.7%). It is also just as important to demonstrate a low false-negative rate (normal LV EF by the Vivio, but an abnormal LV EF by CMR), as it would be a missed opportunity to intervene in patients with asymptomatic disease; fortunately, this proportion was low (14.3%). We do acknowledge that given the false-positivity rate of 7.6% with the Vivio, a proportion of survivors would likely need to undergo additional costly follow-up tests; fortunately, that proportion was low. As expected, there was a dose-dependent increase in the risk of cardiac dysfunction by anthracycline exposure, with a nearly 5-fold increased risk in survivors treated with high-dose ( $\geq 250$  mg/m<sup>2</sup>) anthracycline compared with those treated with lower (<250 mg/m<sup>2</sup>) doses.

For anthracycline-exposed childhood cancer survivors, the cost of echocardiography (using the existing guideline recommendations) is the greatest contributor to lifetime cardiac screening cost (>\$55,000 per person; ref. 31). Of the estimated 400,000 childhood cancer survivors living in the United States, nearly 60% have been exposed to anthracyclines, and thus routinely undergo echocardiographic screening (~\$13 billion in lifetime costs; refs. 1, 25). For adults treated with cardiotoxic therapies (hematologic malignancy, breast cancer), the need to pursue cost-reduction strategies without compromising quality of cancer care is especially urgent, because the combined healthcare costs for this subset of patients are expected to reach \$50 billion/year by the year 2020 (32). As such, it is imperative that accurate yet inexpensive alternatives be pursued for monitoring of these patients. The handheld wireless BLE-enabled device examined in the current study could permit routine monitoring of LV EF in at-risk cancer survivors at a fraction of the current cost (~\$80 per use of app/device) and increase access to advanced cardiac monitoring globally to anyone owning a smart phone. Additional studies are needed to examine the health-economic implications of remote screening in these survivors, taking into consideration the need for real-time interpretation of screening results and efficacy of interventions to minimize the long-term burden of chronic disease in patients with asymptomatic disease.

The findings from the current study need to be considered in the context of its limitations. This was a single-center study that relied exclusively on LV EF for the diagnosis of cardiac dysfunction because it is the most frequently used and easily reproducible parameter across a variety of imaging platforms (33). Several other cardiac imaging parameters such as LV wall stress, thickness to dimension ratio, and diastolic dysfunction have been used to

describe cardiac dysfunction in childhood cancer survivors (33–35). The long-term implications of many of these early ventricular changes on future heart failure risk are not known, and their correlation with more subtle measurements obtained from the Vivio may be the focus of future investigations. For the current study, we did not grade the severity of valvular defects that could be identified by echocardiography or CMR but not by Vivio because it was not considered a primary endpoint. That said, there were no new clinically significant (actionable) valvular or structural (e.g., pericardial effusions) abnormalities detected by either echocardiography or CMR during the conduct of the study. We acknowledge that despite comparable mean LV EF between the Vivio and CMR, there was only a modest correlation ( $r = 0.44$ ,  $P < 0.01$ ) between the two screening approaches, which may be due to the clustered distribution (EF range, 38%–68%) of measurements in this asymptomatic population. In a recent study of nononcology patients that included patients with clinical heart failure, the correlation between the same intrinsic frequency (IF) waveform-based measurements and CMR was 0.74 (13), likely due to the wider distribution of LV EF (range, 8%–73%) in these patients.

It is worth noting that Vivio-based measurements were performed by trained research personnel, and 8 (3.8%) participants were excluded from our analysis because of low quality waveform recordings that did not pass the blinded technicians' standards for acceptable cycles. The low quality of waveforms could be due to interindividual differences in carotid anatomy or extrinsic factors such as operator measurement technique; this remains an area of ongoing investigation with the manufacturers of Vivio. As such, we are not able to comment on the logistics, quality control, and training that would be required prior to its implementation in routine clinical care. Additional studies are needed to examine the optimal setting for Vivio-based screening (e.g., primary care office, survivorship clinic, self-screening) and to determine the survivor population that would derive the greatest benefit from mHealth-based screening. Finally, we acknowledge that arterial stiffness, either due to aging or extrinsic exposures (chemotherapy and/or radiotherapy), can modify the arterial pulse waveform obtained from the device (36–39). However, arterial stiffness does not limit our ability to perform a measurement of LV EF by Vivio because in larger blood vessels such as the aorta or carotid artery, where the waveform data were captured by Vivio, the wall displacement waveform has the same shape as the arterial pressure waveform (13).

In conclusion, the LV EF measurements obtained from the Vivio were more accurate than those obtained from the standard-

of-care approach (2D echocardiography) and were comparable with the costlier yet gold-standard measures obtained from CMR. The findings from this study may facilitate the development of population-based cardiovascular disease research in large cohorts of cancer survivors at a fraction of the cost and resources necessary to conduct such studies. Importantly, once validated, this technology has the potential to change the day-to-day practice of clinicians caring for the >550,000 nononcology patients diagnosed with heart failure each year, allowing real-time monitoring and management of their heart disease without the lag-time between imaging and interpretation of results.

### Disclosure of Potential Conflicts of Interest

D. Rinderknecht is an employee of and is a consultant/advisory board member for Avicena, LLC, and has ownership interests (including patents) at Caltech. P. Tavallali has ownership interests (including patents) at Units. N. Pahlevan has ownership interests (including patents) at and is a consultant/advisory board member for Avicena LLC. M. Gharib has ownership interests (including patents) at Avicena LLC. No potential conflicts of interest were disclosed by the other authors.

### Authors' Contributions

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