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● *Original Contribution*

EVALUATION OF CORONARY ARTERY DISEASE USING MYOCARDIAL ELASTOGRAPHY WITH DIVERGING WAVE IMAGING: VALIDATION AGAINST MYOCARDIAL PERFUSION IMAGING AND CORONARY ANGIOGRAPHY

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Abstract—Myocardial elastography (ME) is an ultrasound-based technique that can image 2-D myocardial strains. The objectives of this study were to illustrate that 2-D myocardial strains can be imaged with diverging wave imaging and differ, on average, between normal and coronary artery disease (CAD) patients. In this study, 66 patients with symptoms of CAD were imaged with myocardial elastography before a nuclear stress test or an invasive coronary angiography. Radial cumulative strains were estimated in all patients. The end-systolic radial strain in the total cross section of the myocardium was significantly higher in normal patients (17.9 ± 8.7%) than in patients with reversible perfusion defect (6.2 ± 9.3%, $p < 0.001$) and patients with significant (−0.9 ± 7.4%, $p < 0.001$) and non-significant (3.7 ± 5.7%, $p < 0.01$) lesions. End-systolic radial strain in the left anterior descending, left circumflex and right coronary artery territory was found to be significantly higher in normal patients than in CAD patients. These preliminary findings indicate that end-systolic radial strain measured with ME is higher on average in healthy persons than in CAD patients and that ME has the potential to be used for non-invasive, radiation-free early detection of CAD. (E-mail: Ek2191@columbia.edu) © 2017 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Cardiac strain imaging, Diverging wave imaging, Coronary artery disease, Myocardial perfusion imaging, Coronary angiography.**

INTRODUCTION

Coronary artery disease (CAD) is characterized by an insufficient blood flow in the coronary arteries and can lead to heart attack and myocardial infarct. It is the leading cause of death worldwide, with 8.1 million deaths in 2013 (Roth et al. 2015), and accounted for approximately 1 of every 7 deaths in the United States in 2011 (Mozaffarian et al. 2015). Various methods are used to diagnose ischemia, such as electrocardiogram (ECG) stress testing, stress echocardiography and nuclear stress tests, or to assess coronary anatomy using coronary computed tomography angiography or magnetic resonance coronary angiography (Montalescot et al. 2013). Stress echocardiography is an ultrasound technique and therefore has the advantages of portability, low risk and of high temporal resolution. However, it requires the myocardium to be stressed either by exercising or pharmacologically and is based mainly on a visual assessment of wall motion abnormalities, which is subjective. Studies have focused on left ventricular systolic function, as it has been reported to be a strong predictor of long-term survival in patients affected by various cardiac diseases (Svealv et al. 2008; Vasan et al. 1999).

Echocardiographic strain imaging has been developed as an ultrasound-based method to objectively and quantitatively assess myocardial deformation during stress or at rest (Gaibazzi et al. 2014; Zuo et al. 2015). Strain imaging offers the advantage of distinguishing tissue motion with deformation from tissue motion without significant deformation, and several studies

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have reported that strain and strain rate imaging are sensitive to myocardial damage after myocardial ischemia or infarction (Edvardsen et al. 2001; Voigt et al. 2003; Weidemann et al. 2007; Winter et al. 2007). The two commercially available cardiac strain imaging techniques are tissue Doppler imaging (TDI) (Hoffmann et al. 2010; Urheim et al. 2000) and speckle tracking echocardiography (STE) (Biering-Sorensen et al. 2014; Gaibazzi et al. 2014). However, TDI is angle- dependent and has low spatial resolution, and STE is performed with B-mode images, which are based on the envelope of the radiofrequency (RF) signals. Previous studies have indicated that the RF signals provide better performance than envelope signals for tissue deformation estimation (Alam and Ophir 1997; Ma and Varghese 2013). Myocardial elastography (ME) is an angle-independent technique for 2-D myocardial strain imaging at high temporal resolution using RF signals (Zervantonakis et al. 2007). This technique has been validated against tagged magnetic resonance imaging and was found to be able to differentiate normal from reperfused myocardium (Lee et al. 2008). A more recent study indicated that ME is capable of detecting, identifying and characterizing down to 40% blood flow reduction in the left anterior descending artery (LAD) of a canine model *in vivo* (Lee et al. 2011). In these previous studies, high frame rates were achieved while maintaining a high beam density by using ECG gating to assemble small sectors of RF signals acquired at different heartbeats into a full echocardiographic view. Not only can this composite sector data acquisition cause mismatches between sectors that can lead to motion artifacts, but also requires the patients to hold their breath during the 20-s duration of acquisition to minimize motion artifacts, which can be challenging for diseased patients.

In this study, the performance of ME by acquiring RF signals at high frame rates during a single heart cycle was investigated. To acquire the full echocardiographic view during a single heart cycle at high frame rate, diverging wave imaging was used. Previous studies have reported that diverging wave imaging can be used to image the heart with high contrast at high temporal resolution (Papadacci et al. 2014) or follow the propagation of the electromechanical wave in the heart at high temporal resolution by estimating inter-frame strains (Provost et al. 2013) and was validated against electrical mapping (Grondin et al. 2016). Diverging wave imaging has also been used to image cardiac end-systolic cumulative axial strains in patients with an intracardiac transducer to differentiate healthy tissue from RF lesion (Grondin et al. 2015). The feasibility and precision of estimating axial and lateral cardiac strain using diverging wave imaging has also been illustrated in healthy volunteers, but without accumulating the strain over systole (Bunting et al. 2014). However, the use of diverging wave imaging for investigating normal and CAD patients by comparing end-systolic accumulated cardiac strain has not yet been investigated.

The objectives of this study were to illustrate that 2-D myocardial strains can be imaged in normal and CAD patients with diverging wave imaging and to investigate the difference in end-systolic radial strains measured between normal and CAD patients.

METHODS

Study population

In this study, the end-systolic radial strain estimated with ME was compared with two widely used techniques to diagnose CAD. Patients with symptoms of CAD and scheduled for a nuclear stress test or an invasive coronary angiography were screened. Patients with prior known myocardial infarct, stent, bypass surgery, heart transplants, severe aortic stenosis, hypertrophic heart, weight $>$220 pounds or a poor acoustic window were excluded from the study. All patients who did not have those exclusion criteria and who gave their informed consent were recruited. Of the 66 patients recruited for this study, 17 were assessed by coronary angiography and 49 were assessed by nuclear perfusion imaging. The study protocol was approved by an institutional review board of Columbia University, and informed consent was obtained before the study.

Myocardial elastography

The patients were scanned at rest with ultrasound before and on the same day as their nuclear stress test or angiography. None of the patients were sedated before the ultrasound scan. The heart was imaged in short-axis view at the basal, mid- and apical levels. A 2.5-MHz center frequency transducer (P4-2, ATL/Philips, Andover, MA, USA) operated by a Verasonics system (V-1, Verasonics, Kirkland, WA, USA) was used to scan the patients. The ECG signal was acquired synchronously with the ultrasound data using an ECG unit (77804 A, HP, Palo Alto, CA, USA) connected to a data acquisition system (NI USB-6210, National Instruments, Austin, TX, USA) and triggered by the Verasonics system. To obtain a large field of view at high frame rate (2000 Hz), diverging wave imaging was used by placing the focus 10 mm behind the surface of the transducer (Provost et al. 2011, 2013). Channel RF data were acquired at 2000 Hz on the 64 elements of the probe during 2 s and sampled at 10 MHz. A standard delay-and-sum method was used to reconstruct the entire image for each single diverging beam transmit (Grondin et al. 2015). The image was reconstructed on a polar grid of 256 lines, sampled