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● *Original Contribution*

# MEASUREMENT OF MYOCARDIAL PERFUSION AND INFARCTION SIZE USING COMPUTER-AIDED DIAGNOSIS SYSTEM FOR MYOCARDIAL CONTRAST ECHOCARDIOGRAPHY

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**Abstract—Proper evaluation of myocardial microvascular perfusion and assessment of infarct size is critical for clinicians. We have developed a novel computer-aided diagnosis (CAD) approach for myocardial contrast echocardiography (MCE) to measure myocardial perfusion and infarct size. Rabbits underwent 15 min of coronary occlusion followed by reperfusion (group I, n = 15) or 60 min of coronary occlusion followed by reperfusion (group II, n = 15). Myocardial contrast echocardiography was performed before and 7 d after ischemia/reperfusion, and images were analyzed with the CAD system on the basis of eliminating particle swarm optimization clustering analysis. The myocardium was quickly and accurately detected using contrast-enhanced images, myocardial perfusion was quantitatively calibrated and a color-coded map calibrated by contrast intensity and automatically produced by the CAD system was used to outline the infarction region. Calibrated contrast intensity was significantly lower in infarct regions than in non-infarct regions, allowing differentiation of abnormal and normal myocardial perfusion. Receiver operating characteristic curve analysis documented that −54-pixel contrast intensity was an optimal cutoff point for the identification of infarcted myocardium with a sensitivity of 95.45% and specificity of 87.50%. Infarct sizes obtained using myocardial perfusion defect analysis of original contrast images and the contrast intensity-based color-coded map in computerized images were compared with infarct sizes measured using triphenyltetrazolium chloride staining. Use of the proposed CAD approach provided observers with more information. The infarct sizes obtained with myocardial perfusion defect analysis, the contrast intensity-based color-coded map and triphenyltetrazolium chloride staining were 23.72 ± 8.41%, 21.77 ± 7.8% and 18.21 ± 4.40% (% left ventricle) respectively ($p > 0.05$), indicating that computerized myocardial contrast echocardiography can accurately measure infarct size. On the basis of the results, we believe the CAD method can quickly and automatically measure myocardial perfusion and infarct size and will, it is hoped, be very helpful in clinical therapeutics.**
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***Key Words:*** **Computer-aided diagnosis, Myocardial contrast echocardiography, Myocardial perfusion, Myocardial infarction, Infarct size.**

## INTRODUCTION

Myocardial infarction (MI) is a serious complication of ischemic heart disease. Furthermore, after MI, the infarcted area can be gradually extended by the subsequent death of cardiomyocytes and vascular cells in the border area. Post-infarction injury can cause cardiac cavity dilation and negative remodeling, eventually leading to heart failure (Kuswardhani & Soejitno, 2011). The key to reducing the mortality associated with MI is to limit and reduce infarct size (De Luca et al. 2004; Gerczuk & Kloner, 2012). A reliable and reproducible method of infarct size assessment is important for deciphering mechanisms underlying MI and for developing and evaluating treatment strategies (Redfors et al. 2012). Moreover, the best approach to determining whether myocardium has been successfully reperfused after an acute MI is assessment of microvascular integrity, which predicts the outcome in patients with a first acute myocardial infarction (Fisher et al. 2002; Ito 2012). Despite the presence of an open artery, myocardial perfusion may not be achieved because of

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microvascular disruption ("no reflow phenomenon") (Ito 2012; Ugander et al. 2012). Therefore, assessing myocardial perfusion and defining infarction size are critical in the study of morphologic and functional repercussions after infarction (Przyklenk, 2013).

Echocardiography is a non-invasive diagnostic technique that provides information regarding cardiac function and hemodynamics. It is the most frequently used cardiovascular diagnostic test after electrocardiography and chest X-ray (Esmaeilzadeh et al. 2013). Several echocardiographic methods and technologies have been developed to aid in the evaluation of myocardial infarct size, such as speckle-tracking echocardiography (Bauer et al. 2011; Peng et al. 2009) and wall shear stress values, which are used to evaluate wall motion and indirectly assess infarct size (Yuan et al. 2011). 3-D echocardiography has been used to assess left ventricular wall motion abnormalities in a mouse model of MI (Streiff et al. 2015). Although previous studies have used available echocardiographic techniques to evaluate infarct size, most of these methods have relied on visual analysis, leading to errors caused by operator subjectivity. With the development of computer applications, many ultrasonic tools based on computer-aided diagnosis (CAD) technologies were developed to automate the identification of infarcted myocardium (Sudarshan et al. 2014). However, it remains a challenge for CAD systems to properly automate the segmentation of echocardiographic images. Many approaches using echocardiographic images have been proposed to identify and segment the ventricular cavity (*i.e.*, endocardium) (Nandagopalan et al. 2013; Sigit et al. 2011), the epicardial boundary (Alessandrini et al. 2013, Seng et al. 2011) and the full myocardium (Chalana et al. 1996; Deopujari et al., 2011; Dietenbeck et al. 2014). Although these methods are useful, most of them are applicable only to 2-D echocardiography images. Furthermore, they do not evaluate and assess infarction size or myocardial perfusion.

Myocardial contrast echocardiography (MCE) is a useful method that has been used to obtain new information for the diagnosis of both MI and myocardial ischemia (Dourado et al. 2003; Lafitte et al. 2002; Porter et al. 1995; Swinburn et al. 2001). Because the contrast agent used in MCE has a rheology similar to that of red blood cells within the microcirculation, MCE can also assess the extent of myocardial capillary perfusion after thrombolytic therapy or percutaneous coronary intervention (Caldas et al. 2004; Ito 2012; Lepper et al. 2000; Trindade et al. 2013). However, computer-aided methodologies for this new technology are in their infancy, and non-perfused regions must be demarcated manually by visual qualitative analysis. The accuracy of such analysis depends on the investigators' experience and their ability to distinguish artifacts from actual perfusion defects. As such, it is evident that standardization and automation of MCE-based myocardial perfusion quantification and infarct size evaluation constitute a critical step in the development of the technology. Few studies have addressed the segmentation of contrast images (Yamada et al. 2005; Yano et al. 2004; Zwirn et al. 2006).

In this article, we document a novel CAD system applicable to MCE image segmentation and based on eliminating particle swarm optimization clustering analysis. The purpose of this study was to quantitatively assess the myocardial microcirculation perfusion and automatically measure infarct size using the CAD system.

## METHODS

### *Animal model experimental protocols*

All animal procedures were approved by the Institutional Animal Care Committee of the Second Affiliated Hospital of Harbin Medical University, Heilongjiang Province, China. All experiments followed the *Guide for The Care and Use of Laboratory Animals* published by the U.S. National Institutes of Health (NIH Publication 85-23, revised 1996).

In this study, 30 male rabbits (2.5 ± 0.5 kg) were anesthetized with sodium pentobarbital (30 mg/kg weight, intravenously). Anesthesia was maintained throughout the whole experiment, and electrocardiography was continuously monitored from limb leads. After baseline images were obtained, a left thoracotomy was performed to open the chest, a pericardial cradle was created and the heart was exposed. The left ventricular branch of the left circumflex coronary artery was isolated and occluded with a 7-O silk snare, which allowed later release to facilitate reperfusion. The rabbits underwent 15 min of coronary occlusion followed by reperfusion (group I, n = 15) or 60 min of coronary occlusion followed by reperfusion (group II, n = 15). The chest was closed in layers, and a small tube was left in the thorax to evacuate air and fluids after surgery.

### *MCE data acquisition*

Myocardial contrast echocardiography was performed using an ultrasound scanner (Vivid 7, GE Healthcare, Milwaukee, WI, USA) equipped with a 7S transducer (5–8 MHz) before and 7 d after induction of ischemia/reperfusion (I/R) injury. A Styrofoam board was tilted to maintain the rabbit in the left lateral decubitus position during image acquisition. Contrast agent (sulfur hexafluoride phospholipid-encapsulated microbubbles [SonoVue, Bracco, Milan, Italy]) was used to enhance the delineation of the left ventricular border. The ultrasound system was adjusted for mechanical index (mechanical index = 0.2); time gain compensation and

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