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● *Original Contribution*

NON-INVASIVE IDENTIFICATION OF VULNERABLE ATHEROSCLEROTIC PLAQUES USING TEXTURE ANALYSIS IN ULTRASOUND CAROTID ELASTOGRAPHY: AN *IN VIVO* FEASIBILITY STUDY VALIDATED BY MAGNETIC RESONANCE IMAGING

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Abstract—The aims of this study were to quantify the textural information of strain rate images in ultrasound carotid elastography and evaluate the feasibility of using the textural features in discriminating stable and vulnerable plaques with magnetic resonance imaging as an *in vivo* reference. Ultrasound radiofrequency data were acquired in 80 carotid plaques from 52 patients, mainly in the longitudinal imaging view, and axial strain rate images were estimated with an ultrasound carotid elastography technique based on an optical flow algorithm. Four textural features of strain rate images—contrast, homogeneity, correlation and angular second moment—were derived based on the gray-level co-occurrence matrix in plaque regions to quantify the deformation distribution pattern. Conventional elastographic indices based on the magnitude of the absolute strain rate, such as the maximum, mean, median, standard deviation and 99th percentile of the axial strain rate, were also obtained for comparison. Composition measurement with magnetic resonance imaging identified 30 plaques as vulnerable and the other 50 as stable. The four textural features, as well as the magnitude of strain rate images, significantly differed between the two groups of plaques. The best performing features for plaque classification were found to be the contrast and 99th percentile of the absolute strain rate, with a comparative area under the receiver operating characteristic curve of 0.81; a slightly higher maximum accuracy of plaque classification can be achieved by the textural feature of contrast (83.8% vs. 81.3%). The results indicate that the use of texture analysis in plaque classification is feasible and that larger local deformations and higher level of complexity in deformation patterns (associated with the elastic or stiffness heterogeneity of plaque tissues) are more likely to occur in vulnerable plaques. (E-mail: luo_jianwen@tsinghua.edu.cn) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Carotid atherosclerotic plaque, Elastography, Magnetic resonance imaging, Plaque classification, Texture analysis, Vulnerability.**

INTRODUCTION

Rupture of carotid atherosclerotic plaques is one of the major causes of cerebrovascular events (Mendel et al. 2002). Therefore, quantitative characterization of plaques and identification of unstable plaques before the events occur are essential for disease prevention and treatment decisions. It is now widely accepted that plaques with a large lipid-rich necrotic core (LRNC) covered by a thin fibrous cap, intra-plaque hemorrhage (IPH), inflammation or neovasculature are more susceptible to rupture (Falk et al. 1995; Finn et al. 2010). Magnetic resonance imaging (MRI) is currently the preferred imaging technique, with the capability of assessing almost all these critical features of vulnerable plaques, and has been validated histologically with endarterectomy specimens (Cai et al. 2002; Saam et al. 2005; Yuan et al. 2001). However, MRI examination is relatively expensive and time consuming, which limits its application in screening of large populations. Ultrasound imaging is inexpensive, widely available, time efficient and readily applicable to asymptomatic populations. Thus, methods based on

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ultrasound imaging are also being continuously developed to identify and characterize vulnerable plaques. Because fibrous and calcific tissues are echogenic materials, whereas lipid and blood are rather echolucent, echogenicity patterns and textural analysis of the plaques on ultrasound B-mode images have been widely used in an attempt to assess the plaque compositions and to discriminate symptomatic from asymptomatic plaques (Christodoulou et al. 2003; Golemati et al. 2013; Grogan et al. 2005; Kanber et al. 2013; Wilhjelm et al. 1998).

One significant advantage of ultrasound imaging compared with other imaging modalities is the high temporal resolution, which allows estimation of tissue motion and deformation with high sensitivity, accuracy and precision. Consequently, evaluation of the mechanical properties of carotid plaques based on motion and deformation estimation with ultrasound imaging provides a different method of plaque assessment. Abnormal plaque motion, such as fine trembling and discrepant motion pattern of the plaque tissues, has been observed to be associated with vulnerable plaques in the literature (Kume et al. 2010; Meairs and Hennerici 1999; Muraki et al. 2016). On the other hand, the main compositions of plaque have different mechanical properties (*e.g.*, elasticity), with fatty tissues being much softer than fibrous tissues (Chai et al. 2013; Lee et al. 1992). Therefore, the deformation is expected to be larger in the vulnerable plaque with softer composition (such as large LRNC and IPH). Ultrasound carotid elastography has been proposed as a technique for mapping tissue deformation by imaging the strain (rate) distributions of the plaque within the ultrasound imaging plane.

The basic principle underlying carotid elastography is that plaque motion and deformation are induced by the physiologic variation in blood pressure, and motion estimation algorithms, such as cross-correlation and optical flow methods, can be used to detect such motion (*i.e.*, displacement and velocity) and deformation (*i.e.*, strain and strain rate) based on the acquired ultrasound images. Various studies have been performed on the elastography of plaques indicating the feasibility of the technique in plaque characterization and risk stratification (de Korte et al. 2000; Hansen et al. 2009; Huang et al. 2016; Kanai et al. 2003; Korukonda and Doyley 2012; Maurice et al. 2004; Ribbers et al. 2007; Shapo et al. 1996; Shi et al. 2008; Wan et al. 2014; Wang et al. 2014; Widman et al. 2015a; Zhang et al. 2015a). The strain distribution of plaque tissues is associated with the stiffness distribution of plaque composition, and higher local strain values are found in softer regions of the plaque (Bonnefous et al. 1996; de Korte et al. 2000; Kanai et al. 2003). Recently, elastography of carotid plaque was compared with MRI, which provided further *in vivo* evidence supporting the usefulness of the technique (Huang et al. 2016; Naim et al. 2013).

Because vulnerable plaques are generally softer than stable plaques (de Korte et al. 2011; Kanai et al. 2003), quantitative indices for plaque assessment are typically derived from the magnitude of plaque deformation, such as the maximum, median and minimum values of local strain or spatially averaged strain over the whole plaque (Huang et al. 2016; Maurice et al. 2008; Naim et al. 2013; Wang et al. 2014; Zhang et al. 2015a). Evidence also suggests the potential use of compositional or elastic heterogeneity in plaque assessment (Box et al. 2007; Tracqui et al. 2011). The abnormal and complex motion of plaque tissues observed in vulnerable plaques reported in the literature (Kume et al. 2010; Meairs and Hennerici 1999; Muraki et al. 2016) may also be a consequence of a heterogeneous pattern of plaque compositions and the non-uniform stress caused by blood pressure variation and complex structure. In a previous study, we also found that both positive (expansion) and negative (compression) strain rates were present simultaneously in most vulnerable plaques, and the strain rate distributions of vulnerable plaques appeared to be less uniform compared with those of stable plaques (Huang et al. 2016). Therefore, we hypothesize that, in addition to a larger magnitude of strain (rate), higher level of strain (rate) heterogeneity is associated with vulnerable carotid atherosclerotic plaques. The aim of this study was to quantify the strain rate distribution of atherosclerotic plaques in carotid elastography using texture analysis, and to evaluate its feasibility in discriminating stable from vulnerable plaques using MRI results as an *in vivo* reference.

METHODS

The experimental protocol, including ultrasound and MRI examination, data acquisition, ultrasound elastography and the MRI review process, has been previously described; more details are given by Huang et al. (2016).

Study population

Participants without major cardiovascular events, including heart attack, stroke and myocardial infarction, within the previous 6 months, were recruited from a community study called Cardiovascular Risk of Old Population (CROP). This study was approved by the institutional review board of the Second Affiliated Hospital of Tsinghua University, and informed consent was obtained from each participant. Participants who had moderate atherosclerotic plaques on either side of the carotid artery as verified by ultrasound imaging were