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● *Original Contribution*

CORRELATION OF COGNITIVE FUNCTION WITH ULTRASOUND STRAIN INDICES IN CAROTID PLAQUE

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Abstract—Instability in carotid vulnerable plaque can generate cerebral micro-emboli, which may be related to both stroke and eventual cognitive abnormality. Strain imaging to detect plaque vulnerability based on regions with large strain fluctuations, with arterial pulsation, may be able to determine the risk of cognitive impairment. Plaque instability may be characterized by increased strain variations over a cardiac cycle. Radiofrequency signals for ultrasound strain imaging were acquired from the carotid arteries of 24 human patients using a Siemens Antares with a VFX 13-5 linear array transducer. These patients underwent standardized cognitive assessment (Repeatable Battery for the Assessment of Neuropsychological Status [RBANS]). Plaque regions were segmented by a radiologist at end-diastole using the Medical Imaging Interaction Toolkit. A hierarchical block-matching motion tracking algorithm was used to estimate the cumulated axial, lateral and shear strains within the imaging plane. The maximum, minimum and peak-to-peak strain indices in the plaque computed from the mean cumulated strain over a small region of interest in the plaque with large deformations were obtained. The maximum and peak-to-peak mean cumulated strain indices over the entire plaque region were also computed. All strain indices were then correlated with RBANS Total performance. Overall cognitive performance (RBANS Total) was negatively associated with values of the maximum strain and the peak-to-peak for axial and lateral strains, respectively. There was no significant correlation between the RBANS Total score and shear strain and strain indices averaged over the entire identified plaque for this group of patients. However, correlation of maximum lateral strain was higher for symptomatic patients ($r = -0.650, p = 0.006$) than for asymptomatic patients ($r = -0.115, p = 0.803$). On the other hand, correlation of maximum axial strain averaged over the entire plaque region was significantly higher for asymptomatic patients ($r = -0.817, p = 0.016$) than for symptomatic patients ($r = -0.224, p = 0.402$). The results reveal a direct relationship between the maximum axial and lateral strain indices in carotid plaque and cognitive impairment. (E-mail: tvarghese@wisc.edu) © 2014 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Elastography, Elasticity imaging, Carotid plaque, Motion tracking, Multi-level, Displacement, Strain, Vascular cognitive dementia.**

INTRODUCTION

Carotid plaque and possible embolic stroke are strongly linked by emboli generated by plaque rupture. Vulnerable plaque is unstable and can be the point of origin of emboli. Its vulnerability may be enhanced when plaque undergoes significant strain variations over the arterial pulsation of the cardiac cycle. Emboli can flow into the vasculature of the brain and cause ischemic events, resulting in stroke, vascular cognitive impairment or both (Whisnant et al. 1990). For every patient who has a stroke, twice as many people experience vascular cognitive impairment (Hachinski et al. 2006). There is evidence that cerebral emboli are significantly correlated with dementia and are associated with a faster decline in cognitive function (Purandare et al. 2006, 2007). It has also been suggested that increased strain in plaque may correlate with cognitive abnormalities (Rocque et al.

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2012), suggesting that it is important to identify patients with vulnerable plaque to prevent future stroke and cognitive impairment.

Characterization of carotid plaque plays an important role in determining its vulnerability to rupture. Ultrasound is a non-invasive option for imaging superior shallow vessels such as the carotid artery. B-mode imaging is commonly used clinically, but is not sufficient to determine plaque vulnerability as it can only separate plaque from normal tissue; it is difficult to differentiate thrombus from surrounding lipidic plaque with B-mode imaging (Noritomi et al. 1997b). Quantitative ultrasound has been used to assess the acoustic properties of tissue, such as attenuation coefficient and integrated backscatter, as differences in acoustic properties may reflect differences in tissue composition (Barzilai et al. 1987; Bridal et al. 1997a, 1997b, 2000; Lee et al. 1998; Noritomi et al. 1997a, 1997b; Picano et al. 1985; Roth et al. 1997; Shi et al. 2008b, 2009; Wilson et al. 1994). Nair et al. (2004) built a classification tree model for autoregressive spectral analysis and developed a real-time automated tissue characterization approach using intravascular ultrasound images of coronary plaque. Their results correspond well to histologic classifications and may lead to virtual histologic evaluations and plaque vulnerability assessments (Nair et al. 2001, 2002, 2004).

Ultrasound strain imaging (Ophir et al. 1991) can be used to estimate the mechanical deformation of plaque and, therefore, can assist in the characterization of plaque vulnerability (Varghese 2009). Most of the research on plaque characterization has focused on intravascular ultrasound because of its high spatial resolution. Intravascular elastography has been used to identify vulnerable plaque both *in vitro* and *in vivo*. Fibrous tissue has lower mean radial strain (0–0.2%) than lipidic tissue (1%–2%) (de Korte et al. 1998, 2000a, 2000b; de Korte and van der Steen 2002). Schaar et al. (2003) used strain imaging and histology separately to identify vulnerable plaque, and plotted strain values against histology indices. They found intra-vascular elastography to be a good diagnostic tool because of its high sensitivity of 88% and specificity of 89%, as determined with receiver operating characteristic (ROC) analysis for a strain threshold of 1.26% (Schaar et al. 2003).

There are fewer studies of non-invasive carotid plaque imaging using elastography and strain imaging (Hansen et al. 2009, 2010; Idzenga et al. 2012; Maurice et al. 2004, 2005, 2008; McCormick et al. 2011, 2012; Ribbers et al. 2007; Schmitt et al. 2007; Shi and Varghese 2007; Shi et al. 2008a). Maurice et al. (2004) proposed a Von Mises parameter to characterize vessel wall and used a Lagrangian speckle model estimator to calculate the strain tensor to estimate axial, lateral, shear and radial strain in plaque. They indicated that their method is reproducible, as the correlation of strain values between the left and right common carotid arteries was significant. Schmitt et al. (2007) implemented the Lagrangian model to estimate strain tensors on both cross-sectional and longitudinal imaging views. They found that axial strain and axial shear strain can provide plaque size information, along with composition and mechanical properties. Ribbers et al. (2007) calculated radial and circumferential strain in two ways: from axial and shear strain and from principal strain. The strain patterns obtained agree with theory, but zero-strain zones exist at diagonal boundaries. Hansen et al. (2010) improved this technique and was able to use an angle-compounding technique to reduce noise artifacts to obtain better radial and circumferential strain estimations from only axial strain. Because ultrasound beams align with the axial direction, it is natural to study plaque in a longitudinal imaging plane. Idzenga et al. (2012) were able to examine longitudinal shear strain in the carotid artery using radiofrequency (RF) data instead of B-mode data. Shi et al. (2008a) developed a multi-level tracking algorithm to calculate displacement and strain and indicated that axial strain and lateral displacement can separate soft from calcified plaque. They therefore hypothesized that this differentiation could help identify vulnerable plaque using cumulated strain indices. McCormick et al. (2012) developed a strain estimation algorithm based on a hierarchical framework using Bayesian regularization to estimate all components of the strain tensor and found that the strain quantities derived from the strain tensor are capable of quantifying the vulnerability of carotid plaque based on cumulated strain indices.

In the study described in this article, we used the algorithms developed by our group to evaluate the distribution and variation of axial, lateral and shear strains for *in vivo* carotid plaque. We focused on the correlation between cognitive function and multiple strain indices.

METHODS

Data acquisition

There were 24 patients who ranged in age from 44 to 79 (mean $\pm$ standard deviation [SD] = 65.88 $\pm$ 8.74). Patients provided informed consent using a protocol approved by the University of Wisconsin—Madison institutional review board before the ultrasound and strain imaging study. Patients underwent ultrasound imaging, which identified significant plaque, and underwent carotid endarterectomy at the University of Wisconsin—Madison Hospitals and Clinics. Additional details on the patients and the different measurements are summarized in Table 1.