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● *Original Contribution*

LONGITUDINAL DISPLACEMENT OF THE CAROTID WALL AND CARDIOVASCULAR RISK FACTORS: ASSOCIATIONS WITH AGING, ADIPOSITY, BLOOD PRESSURE AND PERIODONTAL DISEASE INDEPENDENT OF CROSS-SECTIONAL DISTENSIBILITY AND INTIMA-MEDIA THICKNESS

Guillaume Zahnd,* Didier Vray,* André Sérusclat,† Djhianne Alibay,† Mark Bartold,‡ Alex Brown,§ Marion Durand,|| Lisa M. Jamieson,¶ Kostas Kapellas,¶ Louise J. Maple-Brown,# Kerin O'Dea,** Philippe Moulin,||†† David S. Celermajer,‡‡ and Michael R. Skilton§§

*Université de Lyon, CREATIS, CNRS UMR 5220, INSERM U1044, INSA, Lyon, France; †Department of Radiology, Louis Pradel Hospital, Lyon, France; ‡Colgate Australian Clinical Dental Research Centre, School of Dentistry, University of Adelaide, Adelaide, Australia; §Baker IDI Heart and Diabetes Institute, Alice Springs, Australia; ||Department of Endocrinology, Louis Pradel Hospital, Hospices Civils de Lyon, Université Lyon1, Lyon, France; ¶Australian Research Centre for Population Oral Health, School of Dentistry, University of Adelaide, Adelaide, Australia; #Menzies School of Health Research, Charles Darwin University, Darwin, Australia; **Sansom Institute for Health Research, UniSA, Adelaide, Australia; ††INSERM UMR 1060, Lyon, France; ‡‡Department of Medicine, University of Sydney; and §§Boden Institute of Obesity, Nutrition, Exercise and Eating Disorders, University of Sydney

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Abstract—The recently discovered longitudinal displacement of the common carotid arterial wall (*i.e.*, the motion along the same plane as the blood flow), may be associated with incident cardiovascular events and represents a novel and relevant clinical information. At present, there have only been a few studies that have been conducted to investigate this longitudinal movement. We propose here a method to assess noninvasively the wall bi-dimensional (two-dimensional [2-D], cross-sectional and longitudinal) motion and present an original approach that combines a robust speckle tracking scheme to guidance by minimal path contours segmentation. Our method is well suited to large clinical population studies as it does not necessitate strong imaging prerequisites. The aim of this study is to describe the association between the longitudinal displacement of the carotid arterial wall and cardiovascular risk factors, among which periodontal disease. Some 126 Indigenous Australians with periodontal disease, an emerging risk factor, and 27 healthy age- and sex-matched non-indigenous control subjects had high-resolution ultrasound scans of the common carotid artery. Carotid intima-media thickness and arterial wall 2-D motion were then assessed using our method in ultrasound B-mode sequences. Carotid longitudinal displacement was markedly lower in the periodontal disease group than the control group (geometric mean (IQR): 0.15 mm (0.13) vs. 0.42 mm (0.30), respectively; $p < 0.0001$), independent of cardiovascular risk factors, cross-sectional distensibility and carotid intima-media thickness ($p < 0.0001$). A multivariable model indicated that the strongest correlates of carotid longitudinal displacement in adults with periodontal disease were age (β-coefficient = $-.235$, $p = .03$), waist (β-coefficient = $-.357$, $p = 0.001$), and pulse pressure (β-coefficient = $.175$, $p = 0.07$), independent of other cardiovascular risk factors, cross-sectional distensibility and pulse wave velocity. Carotid longitudinal displacement, estimated with our approach, is impaired in the periodontal disease group, independent of established cardiovascular risk factors and other noninvasive measures of arterial stiffness, and may represent an important marker of cardiovascular risk. (E-mail: guillaume.zahnd@creatis.insa-lyon.fr or michael.skilton@sydney.edu.au)

Key Words: **Arterial stiffness, Atherosclerosis, B-mode ultrasound, Cardiovascular risk factors, Carotid artery, Longitudinal displacement, Motion estimation, Periodontal disease, Segmentation, Speckle tracking.**

INTRODUCTION

Alterations in vascular dynamics, including arterial stiffening, are present decades prior to the onset of clinical cardiovascular events (Celermajer et al. 1992; Whincup

Address correspondence to: Guillaume Zahnd, CREATIS, INSA Lyon, Bât. Blaise Pascal, 7 Av. Jean Capelle, 69621 Villeurbanne Cedex, France. E-mail: guillaume.zahnd@creatis.insa-lyon.fr or michael.skilton@sydney.edu.au

et al. 2005) and appear to be predictive of cardiovascular events independent of traditional risk factors (Laurent et al. 2001; Weber et al. 2004; Dolan et al. 2006). Cross-sectional (*i.e.* radial) stiffness is a strong contributor to arterial pulse wave velocity (PWV), the current gold standard measure of arterial stiffness. Accordingly, the assessment of diameter change of the common carotid artery through the cardiac cycle is widely used as a measure of localized arterial stiffness (Gamble et al. 1994; Hansen et al. 1995; Jiang et al. 2000).

Nonetheless, these classical methods cannot directly capture the information concerning the specific movement of the arterial wall in the same orientation as the blood. Such longitudinal displacement of the intima-media complex tissues is less likely to influence arterial PWV, however, it may provide relevant additional information concerning arterial stiffness and vascular health than that derived from established methods. Longitudinal displacement of the human arterial wall and its physiologic implications have been characterized by recent studies, namely this phenomenon (1) can be measured noninvasively with precision (Cinthio et al. 2005); (2) has been detailed as a complex triphasic motion pattern with a larger movement against the blood flow during systole and being of the same magnitude as the radial motion (Cinthio et al. 2006); (3) has been demonstrated to be reduced in patients with carotid plaques, coronary artery disease and type 2 diabetes (Svedlund and Gan 2011a, 2011b; Zahnd et al. 2011a); (4) may be predictive of incident cardiovascular events independent of carotid stiffness and carotid atherosclerosis (Svedlund et al. 2011); and, (5) in pigs, undergoes profound changes in response to catecholamines (Ahlgren et al. 2011).

Periodontal disease, an inflammatory disease of the tissues surrounding the teeth, is an emerging independent cardiovascular risk factor (Scannapieco et al. 2003; Bouchard et al. 2010). Periodontal disease is associated with preclinical measures of vascular health including increased subclinical atherosclerosis and arterial endothelial dysfunction (Amar et al. 2003; Beck et al. 2011) but not PWV (Miyaki et al. 2006; Franek et al. 2009). Accordingly, we sought to determine whether carotid longitudinal displacement is altered in adults with periodontal disease, compared with age- and sex-matched healthy control subjects. The periodontal disease group was made up of Indigenous Australians with moderate to severe periodontal disease enrolled in the PerioCardio study (Skilton et al. 2011). Indigenous Australians are at increased risk of premature cardiovascular disease, predominantly because of increased burden of established and emerging cardiovascular risk factors, as opposed to being Indigenous *per se* (O'Dea 1991; Brown et al. 2005). Additionally, periodontal disease is associated with elevated total cholesterol and low high-density lipoprotein cholesterol (HDL-c) (Wu et al. 2000; Buhlin et al. 2003). Thus, we also sought to determine whether any observed difference in carotid longitudinal displacement between the periodontal disease and control groups was potentially because of differences in established cardiovascular risk factors. We also described the association of cardiovascular risk factors with carotid longitudinal displacement within adults with periodontal disease, to further describe the association of specific risk factors and carotid longitudinal displacement.

MATERIALS AND METHODS

Study populations

Subjects with periodontal disease were participants in the PerioCardio study, described in detail elsewhere (Skilton et al. 2011). These participants are Indigenous Australians with moderate to severe periodontal disease, aged ≥25 years, with no known history of cardiovascular disease. The first 126 participants recruited into the PerioCardio study were included in this analysis. One participant had ultrasound scans of insufficient quality to enable assessment of longitudinal displacement (*i.e.*, the interfaces of both walls could not clearly be seen because of the image noise) and, thus, was excluded from analysis.

As a control group, we included 27 age- and sex-matched healthy volunteers from Lyon, France, who were part of a larger study conducted by ourselves and others, in which carotid longitudinal displacement was ascertained using the same technique. Control subjects were healthy, non-smoking adults with no prior history of cardiovascular risk factors (hypercholesterolemia, diabetes, hypertension or family history of cardiovascular events).

Table 1 displays participant characteristics for the periodontal disease and control groups. Informed consent was obtained from all participants and the study was approved by appropriate institutional ethics committees in both Australia (Menzies School of Health Research, Northern Territory Department of Health Human Research Ethics Committee, Central Australian Human Research Ethics Committee, Northern Territory Correctional Services Research Committee, University of Adelaide Human Research Ethics Committee and the Aboriginal Health Council of South Australia) and France (Sud-Est committee).

Acquisition of the carotid artery ultrasound sequences

Ultrasound images for the periodontal disease group were obtained using a portable ultrasound (Sonosite MicroMaxx, Bothell, WA, USA), with a 10–5 MHz linear array transducer, as previously described (Skilton et al. 2011). The B-mode sequence frame rate was 45 fps and the pixel size was 47 μm in both radial and longitudinal directions. Multiple loops of approximately six cardiac cycles duration were obtained for both the right and left common