Ultrasound in Med. & Biol., Vol. 40, No. 10, pp. 2392–2403, 2014

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2014.03.009

● *Original Contribution*

HIGH-DEFINITION IMAGING OF CAROTID ARTERY WALL DYNAMICS

Pieter Kruizinga,* Frits Mastik,* Stijn C. H. van den Oord,*† Arend F. L. Schinkel,† Johannes G. Bosch,* Nico de Jong,*‡§ Gijs van Soest,* and Anton F. W. van der Steen*‡§||

*Department of Biomedical Engineering, Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands; †Department of Cardiology, Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands; ‡Interuniversity Cardiology Institute, Utrecht, The Netherlands; §Delft University of Technology, Delft, The Netherlands; and ||Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China

(*Received* 11 *December* 2013; *revised* 12 *February* 2014; *in final form* 10 *March* 2014)

Abstract—The carotid artery (CA) is central to cardiovascular research, because of the clinical relevance of CA plaques as culprits of stroke and the accessibility of the CA for cardiovascular screening. The viscoelastic state of this artery, essential for clinical evaluation, can be assessed by observing arterial deformation in response to the pressure changes throughout the cardiac cycle. Ultrasound imaging has proven to be an excellent tool to monitor these dynamic deformation processes. We describe how a new technique called high-frame-rate ultrasound imaging captures the tissue deformation dynamics throughout the cardiac cycle in unprecedented detail. Local tissue motion exhibits distinct features of sub-micrometer displacements on a sub-millisecond time scale. We present a high-definition motion analysis technique based on plane wave ultrasound imaging able to capture these features. We validated this method by screening a group of healthy volunteers and compared the results with those for two patients known to have atherosclerosis to illustrate the potential utility of this technique. (E-mail: p.kruizinga@erasmusmc.nl) **© 2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Plane wave imaging, High-frame-rate ultrasound, Carotid artery, Tissue Doppler, Pulse wave velocity.**

INTRODUCTION

The healthy artery wall is a layered structure with nonlinear elastic properties that enable it to sustain rapid and large variations in blood pressure (Shadwick 1999). Muscular arteries, such as the carotid and coronary arteries, respond actively and passively to the systemic pressure cycle, adapting their diameter or tone to physiologic circumstances. Under the influence of age and chemical and mechanical stresses, the artery wall may be affected by atherosclerosis, a systemic inflammatory disease that leads to the formation of plaques consisting of calcifications and lipid-rich necrotic material. Lipid-rich plaques may become unstable and rupture, in which case an atherothrombotic reaction can lead to cerebral or cardiac ischemic events (Carr et al. 1996; Schaar et al. 2003; Shoji et al. 2010; van Popele et al. 2001). Advanced atherosclerosis also compromises vascular function and the elastic response of the arteries in a phenomenon known as arterial stiffening. Loss of elasticity of the arterial wall may result in systemic arterial hypertension (O'Rourke et al. 2002). A full assessment of vascular elasticity, as well as plaque stability, requires mapping of the local biomechanical properties of the artery wall: Atherosclerosis is heterogeneous in its prevalence and severity. Soft plaques are more liable to rupture than stiff ones (de Korte et al. 2002; Grønholdt 1999; Shah 2003), and arterial stiffness varies throughout the body. Local biomechanics can be probed by imaging the tissue velocity in response to the systemic pressure variations.

Those local variations are critical to plaque stability: A rupture will occur if the weakest point lacks sufficient strength to withstand the applied stress, a condition that cannot be gauged by average measurements (Cheng et al. 1993; de Korte et al. 2002; Schaar et al. 2003). Locations with large tissue strain are particularly liable to rupture. The amount of tissue deformation can be obtained by measuring the tissue velocity under varying load (D'Hooge et al. 2000; Heimdal et al. 1998; Schmidt-Trucksäss et al. 1998). In this paper we aim to measure the tissue velocity of the carotid artery (CA) wall. The CA is important because of its high incidence of atherosclerosis, its strong association with cerebrovascular

Address correspondence to: Pieter Kruizinga, PO Box 2040, 3000 CA Rotterdam, The Netherlands. E-mail: p.kruizinga@erasmusmc.nl

events (Grønholdt et al. 2001; Laurent et al. 2006) and the relation between atherosclerosis in the CA and atherosclerosis in other vascular beds, such as the coronary arteries (Hellings et al. 2010; Inaba et al. 2012; Lorenz et al. 2007; Triposkiadis et al. 2005). The CA is also superficially located, making it an ideal imaging target for screening applications.

Arteries can become stiff, losing the ability to support large and rapid pressure variations. The most reliable indicator of arterial stiffness is thought to be arterial pulse wave velocity (PWV) obtained with ultrasound (US) echo tracking (Asmar et al. 1995; Benthin et al. 1991; Hoeks et al. 1990; Laurent et al. 2006; O'Rourke et al. 2002). The propagation speed of the pulse wave (PW), a pressure wave generated by the heart in systole, can be related to arterial elasticity using the Moens–Korteweg equation (Korteweg 1878), whereby stiffening of the arterial wall causes the PW to propagate faster (Hermeling et al. 2007). In recent years, several research groups have refined the quantification of the PWV in the CA using high-frame-rate (HFR) ultrasound (Couade et al. 2011; Eriksson et al. 2002; Hasegawa et al. 2013; Hermeling et al. 2009; Kanai et al. 2000; Luo et al. 2012; Sorensen et al. 2008). Although the techniques developed in these studies adequately measure PWV, they do not transcend the limitation of using a single parameter to describe the overall elastic state of a complete arterial segment, in this case the CA. Such a single parameter assumes a constant elastic state throughout the cardiac cycle and a constant elastic state across the whole region. These two assumptions ignore two important observations. First, because the elastic state of the artery wall varies with blood pressure (Shadwick 1999) and heart rate (Lantelme et al. 2002), the propagation of the arterial pulse wave is non-linear (Couade et al. 2010; Fung 1993). Second, applying an average PWV to an entire arterial segment does not allow for the assessment of local variations in the elastic properties within the wall (Shahmirzadi and Konofagou 2012).

Accurate assessment of arterial disease thus necessitates local evaluation of the tissue dynamics. The typical length scales and tissue velocities involved lead to requirements of high temporal and spatial resolution. In the case of the CA, we want to image the interaction of the incoming phase of any arterial PW with the CA wall over some distance. Considering a PWV of several meters per second (Koivistoinen et al. 2007) and an interaction length on the order of millimeters, we require a modality that can provide frame rates on the order of kilohertz. Given that the tissue velocity during PW interactions is only a few millimeters per second (Eriksson et al. 2002; Luo et al. 2012), we require that the modality is capable of measuring sub-micron displacement. The only imaging tool available today that can fulfill both requirements is HFR ultrasound imaging (Ekroll et al. 2013; Hasegawa and Kanai 2008; Lu 1997; Tanter et al. 2002; Udesen et al. 2008).

Here we present a high-definition motion-analysis technique based on plane-wave US imaging, which allows us to visualize arterial wall dynamics at short time and small spatial scales. We measure arterial wall motion on the basis of instantaneous phase echo differences between successive frames obtained with plane wave US imaging. We illustrate that the first-order difference of the instantaneous phase of the beamformed signals provides an efficient way to measure tissue motion locally. With this method, we can now capture the full dynamics of pressure waves interacting with the CA wall. To test our method, we scanned a group of healthy volunteers ($n = 23$) and patients with CA arteriosclerosis ($n = 2$) using HFR US imaging at an average frame rate of 4.6 kHz. We illustrate that motion in a diseased artery wall with plaque is different from the motion observed in a healthy artery. We also provide proof that this technique can be used to obtain the PWV. The validity of the proposed motion derivation is indicated by the reproducibility and consistency over the volunteers, over several cardiac cycles per volunteer and frame-to-frame motion.

METHODS

With the US technique, the resolution of delay estimation is very good in the direction of the transmit beam (axial motion) and is poor in the direction perpendicular to the beam (lateral motion). We therefore decided to restrict ourselves to axial motion, although it should be noted that there are techniques that can measure the complete tissue displacement vector with US imaging (Ekroll et al. 2013; Jensen and Munk 1998; Tanter et al. 2002). Fortunately, the lateral motion of the CA wall in the longitudinal view is predominantly slow (induced by, *e.g.*, breathing) and easily separated from the rapidly changing axial motion, with the latter intrinsically related to arterial distension (Golemati et al. 2003; Zahnd et al. 2013).

Ultrasound imaging relies on the detection of ultrasonic pulses reflected (and backscattered) by tissue. When tissue moves, the next resulting reflection exhibits a delay with respect to the earlier echoes. Measuring this delay provides a direct tool for assessing tissue motion. Delay estimation in US is often done by cross-correlating the received echoes (Lubinski et al. 1999). Instead of cross-correlating the echoes, we can also use the phase of the signals to determine the delays. The phase can be unwrapped to obtain a measure of the exact location of the echoes along each image line, as proposed by Wilson and Robinson (1982). However, unwrapping may introduce errors as a result of noise when the phase