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● *Original Contribution*

ARTERIAL PHANTOMS WITH REGIONAL VARIATIONS IN WALL STIFFNESS AND THICKNESS

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Abstract—Regional wall stiffening and thickening are two common pathological features of arteries. To account for these two features, we developed a new arterial phantom design framework to facilitate the development of vessel models that contain a lesion segment whose wall stiffness and thickness differ from those of other segments. This new framework is based on multi-part injection molding principles that sequentially casted the lesion segment and the flank segments of the vessel model using molding parts devised with computer-aided design tools. The vessel-mimicking material is created from polyvinyl alcohol cryogel, and its acoustic properties are similar to those of arteries. As a case demonstration, we fabricated a stenosed three-segment phantom composed of a central lesion segment (5.1-mm diameter, 1.95-mm wall thickness, 212.6-kPa elastic modulus) and two flank segments (6.0-mm diameter, 1.5-mm wall thickness, 133.7-kPa elastic modulus). B-mode imaging confirmed the difference in thickness between the lesion segment and flank segments of the phantom. Also, Doppler-based vessel wall displacement analysis revealed that when pulsatile flow was fed through the phantom (carotid pulse; 27 mL/s peak flow rate), the lesion segment distended less compared with the flank segments. Specifically, the three-beat averaged peak wall displacement in the lesion segment was measured as 0.28 mm, and it was significantly smaller than that of the flank segments (0.60 mm). It is anticipated that this new multi-segment arterial phantom can serve as a performance testbed for the evaluation of local arterial stiffness estimation algorithms. (E-mail: alfred.yu@uwaterloo.ca) © 2018 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: **Arterial phantom, Lesion segment, Vessel stiffness, Wall thickness, Regional variation.**

INTRODUCTION

Arterial wall hardening has been well acknowledged to be connected to cardiovascular diseases (Mitchell et al. 2010). This vascular condition is known to contribute to the development of atherosclerosis (Pearson et al. 2003) and peripheral artery disease (Ouriel 2001), and it has been clinically regarded as a major risk factor for stroke (van Sloten et al. 2015) and cognitive impairment (Gorelick et al. 2011). Recognizing such etiological significance, various efforts have been made to devise methods that can non-invasively assess arterial stiffness (Laurent et al. 2006) and, in turn, to derive quantitative indices (*e.g.,* distensibility) that can characterize the extent of arterial hardening (Oliver and Webb 2003). While early diagnostic solutions such as applanation tonometry have focused on rendering overall indicators of arterial stiffness (Segers et al. 2009), newer techniques based on ultrasonics principles have enabled the assessment of regional arterial stiffness over a specific artery segment where local changes in arterial stiffness (*i.e.,* a sign of focal lesion) may appear (Messas et al. 2013). These ultrasound-based techniques generally involve the tracking of arterial pulse waves (Brands et al. 1998; Eriksson et al. 2002; Li et al. 2016; Salles et al. 2015) and guided axial waves (Li et al. 2017) or the use of extrinsically generated shear waves (Couade et al. 2010; He et al. 2017; Trahey et al. 2004). Initial feasibility of some of the proposed methods in vivo has already been reported (Ramnarine et al. 2014; Vappou et al. 2010).

As new diagnostic ultrasound methods are being developed to gauge the local stiffness of an artery, there is an emerging need to develop suitable vascular phantoms that can test the efficacy of a candidate method in detecting local arterial hardening. What is required is not a tissue phantom with manipulatable elastic properties (Hall et al.

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1997; Pavan et al. 2010). Wall-less flow phantoms are also not suitable because they inherently lack a vessel wall (Demitri et al. 2008; Nikitichev et al. 2016; Veltmann et al. 2002; Wang et al. 2017), despite the fact that their vascular geometry can include spiral curves (Yiu and Yu 2017) and anthropomorphic arterial shapes (Ho et al. 2017; Poepping et al. 2002). Instead, it is desirable to construct thin-walled vascular phantoms with local wall stiffening or focal lesion-mimicking features. For this purpose, off-the-shelf tubing (Law et al. 1989) is not an appropriate vessel wall material because its mechanical properties cannot be manipulated and its acoustic properties are significantly different from those for arteries (Hoskins 2008). As well, it is not ideal to manufacture walled phantoms using a single type of wall-mimicking material (Dineley et al. 2006; Frayne et al. 1993; King et al. 2011), because atherosclerosis is typically marked by interspersed tissue stiffening that results in heterogeneous arterial compliance (Falk 2006; Ross 1999). This limitation generally applies to all walled phantoms with uniform mechanical properties, including those that possess anthropomorphic vascular geometry (Chee et al. 2016; Lai et al. 2013; Poepping et al. 2004).

Instead of having a homogenous wall, vascular phantoms may be fabricated with two wall layers (Sjöstrand et al. 2017) or with two wall segments of different elasticity (Li et al. 2016; Maksuti et al. 2016). However, these phantom designs are still fundamentally not intended to resemble local arterial lesions that are marked by focal stiffening and thickening of the vessel wall. An alternative solution is to incorporate inclusion features when constructing the vessel-mimicking wall (Boekhoven et al. 2014; Galluzzo et al. 2015) such that a local wall segment with a different elasticity can be created. Yet, for these phantoms, it is not straightforward to precisely control the focal lesion size and its elastic properties because their fabrication is after all based on needle-based injection of a fatty material such as porcine lard (Boekhoven et al. 2014) or liquefied butter (Galluzzo et al. 2015). Accordingly, it may not be trivial to consistently use these phantoms as investigative tools for the evaluation of local arterial hardening detection methods.

In this article, we present a new framework for developing arterial phantoms that incorporate local wall stiffening and thickening features to mimic focal arterial lesions. The new phantom development protocol has incorporated three novel aspects. First, it is capable of constructing multi-segment vessel models that contain a lesion-mimicking segment at their center and include flank segments with normal arterial properties. Second, it allows the structural parameters of different vessel segments (length and wall thickness) to be controllably specified. Third, it enables the mechanical stiffness (elastic modulus) of different vessel segments to be tuned such that the lesion segment is made stiffer than the flank segments. With such controlled heterogeneity in vessel properties, the arterial phantoms developed using this new protocol are intended to serve as testbeds for performance analysis of existing and new diagnostic ultrasound techniques for local arterial stiffness estimation.

PHANTOM DESIGN METHODS

Our new phantom fabrication protocol comprises three main stages to manufacture an arterial phantom with local stiffening and wall thickening: (i) development of the vessel's lesion segment; (ii) formation of the vessel's flank segments; (iii) phantom construction using the developed vessel tube. It is founded on the concept of multi-part injection molding, whereby three major casting parts were used: vessel core (Fig. 1a), wrapper block (Fig. 1b) and outer mold (Fig. 1c). The details of each stage of fabrication, including the design of casting parts, are described in the following subsections.

Development of lesion segment

Vessel core fabrication. Using the SolidWorks computer-aided design (CAD) software (Dassault Systèmes, Waltham, MA, USA), we first drafted the vessel lumen core needed for arterial phantom construction. As illustrated in Figure 1(a), the vessel lumen core was drafted as a rod-like structure with a length of 300 mm. Its diameter was set to 6.0 mm, as this value corresponded to the average diameter of the common carotid artery (CCA) in adults (Krejza et al. 2006). Accordingly, the drafted vessel core can be considered as an idealized model of the CCA: a part of the vasculature where ultrasound has been reported to have applicability in atherosclerosis diagnostics (Ho 2016). As a disease-mimicking feature, a 15-mm-long stenotic narrowing zone was created around the midpoint of the vessel core (Fig. 2a). The extent of narrowing was defined based on the North American Symptomatic Carotid Endarterectomy Trial criterion that expressed stenosis in the form of a percentage (Smith et al. 1996). Fifteen percent concentric stenosis (*i.e.,* 5.1-mm diameter) was implemented as a proof of concept to simulate a pathological case with early-stage atherosclerosis. The completed vessel core model was physically built using the same 3-D printing protocol that we used previously (Chee et al. 2016; Ho et al. 2017). This task involved the use of an open-source fused deposition modeling system as the 3-D printer (Model DX, Creatbot 3-D Printer, Zhengzhou, China) and the use of polylactic acid thermoplastic as the 3-D printing material. Supporting cylinders were added to the CAD model to provide mechanical support during the 3-D printing process, and they were clipped off afterward to obtain the vessel core replicate (Ho et al. 2017).