Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–23, 2017

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2017.06.002

● *Original Contribution*

DETECTING REGIONAL STIFFNESS CHANGES IN AORTIC ANEURYSMAL GEOMETRIES USING PRESSURE-NORMALIZED STRAIN

Doran S. Mix,*† Ling Yang,‡ Camille C. Johnson,† Nathan Couper,*‡ Ben Zarras,‡ Isaac Arabadjis,† Lauren E. Trakimas,* Michael C. Stoner,* Steven W. Day,† and Michael S. Richards*†

*Division of Vascular Surgery, Department of Surgery, University of Rochester Medical Center, Rochester, New York, USA; †Department of Biomedical Engineering, Rochester Institute of Technology, Rochester, New York, USA; and ‡Department of Biomedical Engineering, University of Rochester, Rochester, New York, USA

(*Received* 4 *October* 2016; *revised* 26 *April* 2017; *in final form* 2 *June* 2017)

Abstract—Transabdominal ultrasound elasticity imaging could improve the assessment of rupture risk for abdominal aortic aneurysms by providing information on the mechanical properties and stress or strain states of vessel walls. We implemented a non-rigid image registration method to visualize the pressure-normalized strain within vascular tissues and adapted it to measure total strain over an entire cardiac cycle. We validated the algorithm's performance with both simulated ultrasound images with known principal strains and anatomically accurate heterogeneous polyvinyl alcohol cryogel vessel phantoms. Patient images of abdominal aortic aneurysm were also used to illustrate the clinical feasibility of our imaging algorithm and the potential value of pressure-normalized strain as a clinical metric. Our results indicated that pressure-normalized strain could be used to identify spatial variations in vessel tissue stiffness. The results of this investigation were sufficiently encouraging to warrant a clinical study measuring abdominal aortic pressure-normalized strain in a patient population with aneurysmal disease. (E-mail: dmix@urmc.rochester.edu) **© 2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Elastography, Elasticity imaging, Strain, Aneurysm, Ultrasound, Registration, Tissue-mimicking phantoms, 3-D printing.**

INTRODUCTION

An abdominal aortic aneurysm (AAA) is a dilation of the primary artery within the abdominal cavity (Vorp 2007). The majority of AAAs are focal and found within the infra-renal segment of the abdominal aorta (Taylor 1994). Since the development of the original reporting standard for arterial aneurysms, an AAA has been defined as a vessel diameter 50% greater than the expected normal vessel diameter (Johnston et al. 1991). Previous computer tomography studies defined the normal abdominal aortic diameter as 1.71 ± 0.06 cm in young women and 2.85 ± 0.04 cm in older men (Ouriel et al. 1992). Many clinical studies and government screening programs have accepted an abdominal aortic diameter >3.0 cm as diagnostic of an AAA (Ashton et al. 2002; Lederle 2000; LeFevre 2014). Although the diagnosis of an abdominal aortic aneurysm is straightforward and can be made using non-invasive imaging techniques, the natural history of a patient's specific AAA is not as precise. The feared sequel of AAA is the free rupture of the vessel wall, with some studies estimating an associated 80% 30-d mortality rate (Powell 2014; Robinson et al. 2016; Starnes et al. 2010).

Currently, surgical repair is the only knows means of preventing rupture of an AAA (Schermerhorn et al. 2008). Surgical aneurysm repair itself is a significant source of mortality and morbidity; thus, an accurate quantification of a patient's rupture risk is required to determine the benefit of elective surgery. Attempts have been made to assign a given patient's risk of AAA rupture using a "maximum size criterion" (Darling et al. 1977; Szilagyi et al. 1966). Although a large body of both clinical trials (De Bruin et al. 2010; Lederle et al. 2002b; Parkinson et al. 2015; Powell et al. 2007;

Address correspondence to: Doran S. Mix, Division of Vascular Surgery, Department of Surgery, University of Rochester Medical Center, 601 Elmwood Avenue, Rochester, NY 14642, USA. E-mail: dmix@urmc.rochester.edu

Schermerhorn et al. 2008; UK Small Aneurysm Trial Participants 1998) and epidemiologic data (Darling et al. 1977; Pleumeekers et al. 1995; Singh 2001) exist to quantify population-based risk of rupture at a given size, each of these studies accepted some degree of rupture mortality within the population (Thompson et al. 2012). A recent single-center report (Skibba et al. 2015) and meta-analysis (Parkinson et al. 2015) suggest that not only do patients rupture below clinically acceptable thresholds for repair, typically ≥5.0 cm in women and ≥5.5 cm in men (Grant et al. 2015), but most patients rupture at sizes substantially greater than the accepted diameters for surgical repair. These data would suggest that prior reports of rupture risk are likely overestimations and that many patients are exposed to surgical risk with possible limited personal benefit (Lederle et al. 2002a). Thus, an improved method for individualized patient rupture risk assessment is needed.

Extensive work has used computer models, such as finite elements (FE), to illustrate that calculations of stress within the aortic wall can provide improved AAA rupture risk prediction (Doyle et al. 2009; Fillinger et al. 2003; Helderman et al. 2008; Maier et al. 2010; Vande Geest et al. 2006). From a biomechanics perspective, the difficulty of any such model is the need for an accurate determination of the material properties of the aortic wall *in vivo*. Additionally, it is known that the aortic wall is a highly heterogeneous structure because of aortic vessel composition (collagen and elastin content and fiber orientation), atherosclerosis and spatial orientation of the aorta (Di Martino et al. 2006; Gasser et al. 2006; Raut et al. 2013; Ruddy et al. 2008; Tavares Monteiro et al. 2014; Vallabhaneni et al. 2004; Zou and Zhang 2012).

Various elastographic imaging methods such as magnetic resonance imaging (MRI) and electrocardiogram-gated computer tomographic angiography have been used to better define patient-specific aortic tissue mechanical properties non-invasively. The clinical utility of these methods has been limited largely by the high cost (Damughatla et al. 2015; Langham et al. 2011), significant ionizing radiation or nephrotoxicity of iodinated radiographic contrast dye (Auricchio et al. 2015; Budovec et al. 2010; Schlicht et al. 2013). As an alternative, ultrasound (US)-based elastographic methods are clinically convenient, as ultrasound is currently used as the standard of care to follow progression of AAA disease (Lee et al. 2009). Additionally, ultrasound-based methods come without the risks of ionizing radiation and can provide high-temporal-resolution data without the need for time-consuming and error-prone spatial reconstruction techniques.

Ultrasound-based elastographic methods can be broadly divided into the two methods for inducing a deformation in tissue: direct (surface induced or physiologic) and radiation force induced (Parker et al. 2012; Wells and Liang 2011). The large amount of tissue between the surface of the abdomen and the retroperitoneum makes freehand displacements of the abdominal aorta impractical and likely painful for patients. Although several studies have looked at the feasibility of performing acoustic radiation force impulse imaging on aneurysm-like geometries, clinical data from such techniques for the abdominal aorta have been limited by the acoustic depths of the aorta (Fahey et al. 2006; Tierney et al. 2011; Trahey et al. 2004).

The pulsatile nature of blood flow provides a physiologic deformation of the aorta that can be used for passive elastographic strain measurements. The Diamove (Teletec, Stockholm, Sweden) was one of the first commercially available cross-correlation-based tracking systems to provide strain measurements from B-mode ultrasound images (Benthin et al. 1991). This system has been used clinically to compare the strain and various calculated measures of stiffness in aneurysms that progress to rupture (Sonesson et al. 1999; Wilson et al. 1998, 2003). Although Sonesson et al. (1999) found no difference in calculated stiffness of aneurysms that progress to rupture in the longitudinal orientation, Wilson et al. (1998, 2003) reported a higher rupture risk in AAAs with lower calculated elastic modules in the axial orientation. Wilson et al. also suggested that aneurysm size was correlated, although poorly ($r^2 = 0.22$), to increases in elastic modulus, suggesting that larger AAAs are stiffer and that rupture risk is more closely associated with aortic material properties than size. Perhaps the greatest limitation of the Diamove system is the use of only two tracked points within the images measured at the posterior wall and anterior wall of the vessel, assuming a simplistic circular model of AAA geometry.

Numerous techniques and methodologies have been published to spatially resolve strain fields in deforming vessels with the end goal of improving knowledge of the tissue mechanics and disease state (Fromageau et al. 2005; Lopata et al. 2009, 2014; Mascarenhas et al. 2016; Vonk et al. 2014). In a novel method of AAA vessel wall tracking from clinical B-mode images, Brekken et al. (2006) used points along one-half the lateral edge of the circumferentially oriented aortic wall, imposing a cubic spline smoothing constraint to the curve to suppress noise. In a similar study, Vonk et al. (2014) tracked the manually segmented walls of a longitudinally oriented AAA and suppressed accumulated noise by using an "adaptive region of interest (ROI) scheme," in which the tracked elements within the ROI were updated based on the displacements. Vonk et al. reported that rapidly growing aneurysms