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● *Original Contribution*

DESIGN AND TESTING OF A SINGLE-ELEMENT ULTRASOUND VISCOELASTOGRAPHY SYSTEM FOR POINT-OF-CARE EDEMA QUANTIFICATION

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Abstract—Management of fluid overload in patients with end-stage renal disease represents a unique challenge to clinical practice because of the lack of accurate and objective measurement methods. Currently, peripheral edema is subjectively assessed by palpation of the patient's extremities, ostensibly a qualitative indication of tissue viscoelastic properties. New robust quantitative estimates of tissue fluid content would allow clinicians to better guide treatment, minimizing reactive treatment decision making. Ultrasound viscoelastography (UVE) can be used to estimate strain in viscoelastic tissue, deriving material properties that can help guide treatment. We are developing and testing a simple, low-cost UVE system using a single-element imaging transducer that is simpler and less computationally demanding than array-based systems. This benchtop validation study tested the feasibility of using the UVE system by measuring the mechanical properties of a tissue-mimicking material under large strains. We generated depth-dependent creep curves and viscoelastic parameter maps of time constants and elastic moduli for the Kelvin model of viscoelasticity. During testing, the UVE system performed well, with mean UVE-measured strain matching standard mechanical testing with maximum absolute errors ≤4%. Motion tracking revealed high correlation and signal-to-noise ratios, indicating that the system is reliable. (E-mail: joebull@umich.edu) © 2016 **World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Creep experiment, Edema, End-stage renal disease, Point-of-care, Poroelasticity, Speckle tracking, Srain imaging, Ultrasound, Viscoelastography.**

INTRODUCTION

End-stage renal disease affects more than 615,000 Americans, with more than 115,000 new cases in 2011 alone and costs totaling $49.3 billion (U.S. Renal Data System 2013). There is no cure for end-stage renal disease, and the median wait time for renal transplant is 2.6 y (U.S. Renal Data System 2013). During that time, patients must undergo regular hemodialysis treatments, and physicians must regularly intervene to control a number of important deficiencies brought on by the loss of kidney function. Because the kidneys can no longer properly control filtration and fluid balance, careful monitoring is necessary to prevent fluid depletion or fluid overload. In particular, fluid overload partially manifested as peripheral edema can accompany life-threatening congestive heart failure. As such, edema is part of the standard clinical assessment for patients. Current techniques for monitoring peripheral edema rely primarily on palpation. Typically, a clinician grasps and compresses an edematous extremity with his or her thumb. The observed indentation is then rated on a semi-quantitative scale from 0 to 4+ to classify the degree of edema. This method is highly imprecise and relies largely on the experience and expertise of the clinician.

Fully quantitative methods based on new technologies have the potential to substantially improve patient fluid balance monitoring by providing a more consistent,

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observer-independent measurement. A number of studies have proposed the use of ultrasound elastography as a potential tool for measuring the mechanical properties of edematous tissue (Adriaenssens et al. 2012; Berry et al. 2008; Kruger et al. 2012; Righetti et al. 2007a). Ultrasound elastography is an imaging technique that allows accurate estimation of internal tissue strain from ultrasound radiofrequency (RF) data (Ophir et al. 1991). Elastography has excelled at imaging the mechanical properties of linearly elastic gelatin phantoms. Biological tissues, however, are rarely linearly elastic. They can more accurately be described using more complex poroelastic (Armstrong et al. 1984), viscoelastic (Fung 1993) or non-linear elasticity models (Hall et al. 2011). Elastography techniques aimed at measuring these types of properties generally fall into three groups based on the material model: poroelastography, viscoelastography and non-linear elastography.

Poroelastography estimates the local effective Poisson's ratio of a material under compression (Berry et al. 2006a, 2006b; Konofagou and Ophir 1998; Righetti et al. 2004, 2005, 2007b). The feasibility of using poroelastography to quantify the properties and strain response of edematous tissue has been reported in lymphedema patients (Berry et al. 2008; Righetti et al. 2007a). Viscoelastography, which has been applied primarily to the imaging of breast tumors, relies on spring-dashpot viscoelastic material models (Insana et al. 2004; Qiu et al. 2008; Sridhar et al. 2007). Standard elastography techniques are first used to estimate the strain field in a compressed medium. The strain data are then fit with an appropriate material model to obtain elastic moduli and viscoelastic time constants that describe the material. Studies employing these techniques have focused primarily on viscoelastic contrast rather than the actual values of the material properties. The notable exception is the 2007 study by Righetti et al. (2007b), which reported the viscoelastic moduli and time constants of a tissue-mimicking material found using axial strain elastograms. Non-linear elastography uses the measured strain field as an input into an inverse problem (Samani and Plewes 2004). The forward mechanical compression problem is solved using non-linear material models, and the solution process is iterated until the forward model matches the measured strain field.

The vast majority of elastography studies are performed using small strains, typically less than 2% (*e.g.*, Berry et al. 2006b; Righetti et al. 2007b). At these strain values, the behavior of tissue is often described as nearly linear. Larger strains could result in a more pronounced non-linear strain response. In addition, larger strains result in increased decorrelation of the ultrasonic speckle pattern, thus reducing the elastographic signal-to-noise ratio (SNR) (Cespedes 1993; Varghese and Ophir 1997). These challenges, however, do not negate the usefulness of elastography imaging in the non-linear regime. The standard clinical examination for edema relies on large strains to differentiate grades of edema, and this convention may be useful for quantifying edema using elastography. Furthermore, errors resulting from speckle decorrelation at large strains can be overcome. By generating a series of incremental strain images from sequential ultrasound frames and then summing these incremental strains, one can arrive at the total strain while minimizing decorrelation errors (O'Donnell et al. 1994).

Another common feature of most elastography studies is the use of array transducers. These transducers generate 2-D images of the tissue in real time. This simple fact makes them generally more useful than single-element transducers, which can image only along one line of sight at a time. Point-of-care applications such as edema monitoring, however, may benefit from the decreased hardware complexity and computational expense associated with single-element systems. This does limit the clinician's ability to image spatial variations within the tissue, but is largely irrelevant for the purposes of edema quantification, where the goal is to estimate bulk properties of the tissue. We have developed a simple, portable ultrasound system specifically for this application. Here we describe the use of this single-element system to quantify the viscoelastic properties of a tissue-mimicking material subjected to large strains.

METHODS

To determine the feasibility of using ultrasound viscoelastography (UVE) measurements to estimate the fluid content of edematous tissue, we conducted two similar experiments. One experiment was a standard creep compression test; the other was a creep compression test with simultaneous UVE measurements. The standard creep compression test served as a gold standard comparison for our UVE measurements. In this section, we outline the procedure used to obtain and process data for each of these experiments.

In all experiments, we used cylindrical samples of extra-firm tofu (Nasoya, Ayer, MA, USA) as an edematous tissue-mimicking phantom. Cylinders were cut from a single block of tofu using a 32-mm-diameter tube of sharpened plastic at room temperature. Next, each cylinder was trimmed to a height of 20 $\pm$ 1 mm. This yielded a total of 12 samples per block of tofu. The samples were relatively uniform in structure, although some macroscale variations in the structure (*e.g.*, larger pores) were visible, as might be expected of a randomly porous material such as tofu. The samples