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● *Original Contribution*

AN ULTRASOUND SURFACE WAVE TECHNIQUE FOR ASSESSING SKIN AND LUNG DISEASES

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Abstract—Systemic sclerosis (SSc) is a multi-organ connective tissue disease characterized by immune dysregulation and organ fibrosis. Severe organ involvement, especially of the skin and lung, is the cause of morbidity and mortality in SSc. Interstitial lung disease (ILD) includes multiple lung disorders in which the lung tissue is fibrotic and stiffened. The purpose of this study was to translate ultrasound surface wave elastography (USWE) for assessing patients with SSc and/or ILD *via* measuring surface wave speeds of both skin and superficial lung tissue. Forty-one patients with both SSc and ILD and 30 healthy patients were enrolled in this study. An external harmonic vibration was used to generate the wave propagation on the skin or lung. Three excitation frequencies of 100, 150 and 200 Hz were used. An ultrasound probe was used to measure the wave propagation in the tissue non-invasively. Surface wave speeds were measured on the forearm and upper arm of both left and right arm, as well as the upper and lower lungs, through six intercostal spaces of patients and healthy patients. Viscoelasticity of the skin was calculated by the wave speed dispersion with frequency using the Voigt model. The magnitudes of surface wave speed and viscoelasticity of patients' skin were significantly higher than those of healthy patients ($p < 0.0001$) for each location and each frequency. The surface wave speeds of patients' lung were significantly higher than those of healthy patients ($p < 0.0001$) for each location and each frequency. USWE is a non-invasive and non-ionizing technique for measuring both skin and lung surface wave speed and may be useful for quantitative assessment of SSc and/or ILD. (E-mail: zhang.xiaoming@mayo.edu) **© 2017 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

Key Words: **Ultrasound surface wave elastography, Skin, Lung, Scleroderma, Interstitial lung disease.**

INTRODUCTION

Systemic sclerosis (SSc), also termed scleroderma, is a multi-organ connective tissue disease characterized by immune dysregulation and organ fibrosis (Steen and Medsger 2000). Thickening of the skin, often the earliest affected organ, is considered an early marker of disease activity in SSc (Steen and Medsger 2000). Severe organ involvement, especially of the skin and lung, is the cause of morbidity and mortality in SSc. The degree of skin involvement is a predictor of mortality (Clements et al. 1990). Improvement in skin stiffness is associated with improved survival in many clinical trials (Steen and Medsger 2001). Patients who do not develop severe organ involvement in the first few years are less likely to develop life-threatening involvement later throughout the course of the disease. The modified Rodnan skin score (MRSS) is the standard skin assessment tool in the majority of clinical studies of SSc (Abignano et al. 2011). Patients with an improved MRSS after 2 y of treatment have improved survival (Steen and Medsger 2001). The MRSS is commonly used as an outcome measure in clinical trials (Clements et al. 2000). However, the MRSS is a palpation method, which is subjective, and thus, its accuracy is user dependent (Clements et al. 1995). Moreover, it is difficult to measure the change in skin stiffness over time using palpation (Postlethwaite et al. 2008).

Skin stiffness can be measured using durometry (Kissin et al. 2006; Merkel et al. 2008), indentation (Boyer et al. 2009; Pailler-Mattei et al. 2008; Serup and Jemec 1995) and cutometers (Hendriks et al. 2006; Smalls et al. 2006). In durometry, a piston-spring-dial handheld

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apparatus is used to measure skin hardness. However, durometry readings are affected by the experience of users. Indentation is the technique of measuring elasticity by indenting the material. The cutometer measures skin displacement in response to a suction force. Because its measurements depend on the interactions between a probe and the skin, deeper skin layers must be measured with larger probes (Hendriks et al. 2006). Notably, these techniques cannot evaluate subcutaneous tissue.

Patients with interstitial lung disease (ILD) have fibrotic and stiff lungs causing symptoms, especially dyspnea, and may eventually lead to respiratory failure (Coultas et al. 1994). Many ILDs typically are distributed in the peripheral, subpleural regions of the lung (Desai et al. 2004; Wells et al. 1993). High-resolution computed tomography (HRCT) is the clinical standard for diagnosing lung fibrosis (Mathieson et al. 1989; Verschakelen 2010), but it substantially increases radiation exposure for patients. Various scanning techniques have been proposed to reduce the dose (Mayo 2009). Intercostal ultrasound can be used to avoid ionizing radiation during follow-up visits (Delle Sedie et al. 2012). However, it is not able to quantify lung stiffness.

Currently, no clinical approach is available to noninvasively quantify and evaluate the progression and development of SSc and ILD. Therefore, there is a pressing need to develop an accurate and reproducible clinical technique for quantification and tracking of the disease and to develop effective treatment for sclerosis and fibrotic disorders (Lott and Girardi 2011). The research described here was aimed at translating an ultrasound surface wave elastography (USWE) technique into clinical use for quantitative assessment of patients with SSc and ILD.

METHOD

Raleigh surface wave equation

Surface wave propagation can be analyzed as wave propagation in a semi-infinite linear elastic medium under a local harmonic excitation on the surface. The equation for wave propagation in an isotropic and elastic medium is (Miller and Pursey 1954)

$$(\lambda+2\mu)\nabla\nabla.\vec{u}-\mu\nabla\times\nabla\times\vec{u}=\rho\frac{\partial^2\vec{u}}{\partial t^2}, \qquad (1)$$

where $\vec{u}$ is the displacement vector, ρ is the mass density and λ and μ are the Lamé coefficients of the medium. For linear viscoelastic material, $\lambda = \lambda_1 + \partial\lambda_2/\partial t$ and $\mu = \mu_1 + \partial\mu_2/\partial t$, where λ_1, λ_2, μ_1 and μ_2 are the coefficients of volume compressibility, volume viscosity, shear elasticity and shear viscosity, respectively.

Surface wave propagation can be solved in the cylindrical polar coordinate system as illustrated in Figure 1. Consider a harmonic force excitation with uniform stress on the surface of the medium in the circular region of $r \le a$.

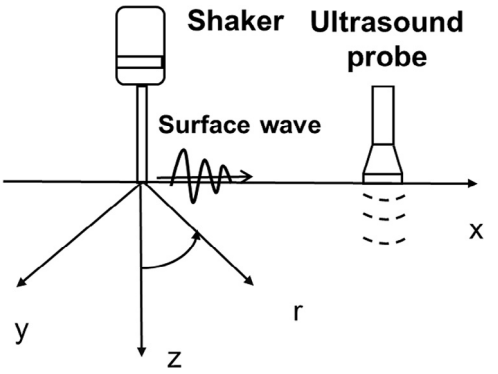

Fig. 1. Schematic of surface wave generation and detection on the skin. The skin surface is on the plane of x- and y-coordinates. The surface wave on the skin is generated by a handheld electromechanical shaker through a ball-tip applicator on the skin. The vibration excitation is typically a 0.1-s harmonic signal at a frequency between 100 and 200 Hz. The resulting surface wave propagation on the skin is measured using an ultrasound probe. A standoff gel pad is used between the ultrasound probe and skin to improve imaging of the skin. The surface wave speed depends on the local elastic properties of the skin and is independent of the location of wave generation.

The displacement fields are derived in the r and z directions at any location in and on the surface of the medium as (Miller and Pursey 1954)

$$\begin{aligned} u_z &= \frac{a}{\mu}\int_0^\infty \frac{\sqrt{(\xi^2-1)}J_1(\xi k_1 a)}{F_0(\xi)}\Big\{2\xi^2 e^{-k_1 z\sqrt{(\xi^2-\eta^2)}} \\ &\quad + (\eta^2-2\xi^2)e^{-k_1 z\sqrt{(\xi^2-1)}}\Big\}J_0(\xi k_1 r)\,d\xi \\ u_r &= \frac{a}{\mu}\int_0^\infty \frac{\xi J_1(\xi k_1 a)}{F_0(\xi)}\Big\{2\sqrt{(\xi^2-1)}\sqrt{(\xi^2-\eta^2)}e^{-k_1 z\sqrt{(\xi^2-\eta^2)}} \\ &\quad + (\eta^2-2\xi^2)e^{-k_1 z\sqrt{(\xi^2-1)}}\Big\}J_1(\xi k_1 r)\,d\xi, \end{aligned} \qquad (2)$$

where a is the radius of the distributed stress, and ξ is the integration parameter in the wavenumber domain, which has been normalized with respect to k_1. The divisor function of the integration functions is $F_0(\xi) = (2\xi^2-\eta^2)^2 - 4\xi^2\sqrt{(\xi^2-1)}\sqrt{(\xi^2-\eta^2)}$, where $\eta = k_2/k_1 = \sqrt{\{2(1-\sigma)/(1-2\sigma)\}}$ and $k_1 = \omega\sqrt{\rho/(\lambda+2\mu)}$, $k_2 = \omega\sqrt{\rho/\mu}$, where ω is the angular frequency, ρ is the density, σ is Poisson's ratio for the medium, k_1 and k_2 denote the wavenumbers for compression and shear wave propagation, respectively, and J_0 and J_1 refer to Bessel functions of the first kind.

The wave displacement fields can be solved with eqn (2). However, using the displacements to estimate the elastic properties of the medium depends on the excitation and boundary conditions. Because the wave propagation is dependent on local medium properties, we used the surface