Quantitative assessment of scleroderma using ultrasound surface wave elastography

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***Abstract* — Skin stiffening is an early biomarker of many systemic fibrotic disorders. The Modified Rodnan Skin Score (MRSS) is considered the gold standard measurement in clinical studies of systemic sclerosis (SSc). However, the MRSS is a palpation method. We have developed a noninvasive ultrasound surface wave elastography (USWE) technique for measuring skin elastic properties. The purpose of this paper is to demonstrate the clinical use of USWE for assessing patients with SSc. In USWE, a low intensity 0.1 second harmonic vibration is generated on the skin of a subject using a handheld vibrator. An ultrasound probe is aligned with the indenter of the vibrator to measure the generated surface wave propagation on the skin. In a prospective clinical study, we measure both skin and lung on patients with SSc and interstitial lung disease (ILD). Significant differences in wave speed between SSc patients and healthy subjects were found. For example, the surface wave speed of the skin is 1.83 ± 0.04 m/s at 100 Hz, 2.33 ± 0.25 m/s at 150 Hz, and 3.04 ± 0.37 m/s at 200 Hz for a healthy subject, and the surface wave speed of the skin is 2.82 ± 0.31 m/s at 100 Hz, 3.60 ± 0.38 m/s at 150 Hz, and 5.36 ± 0.55 m/s at 200 Hz for an age matched SSc patient in the same location. USWE is a noninvasive technique for generating and measuring surface wave propagation on the skin. USWE can provide objective measurement of skin elastic properties in various regions of the body, which may be useful for assessing the status and potentially the progression of SSc.**

Keywords-ultrasound surface wave elastography, skin, scleroderma

I. INTRODUCTION

Systemic sclerosis (SSc), also termed scleroderma, is a multi-organ connective tissue disease characterized by immune dysregulation and organ fibrosis [1]. Thickening of the skin, often the earliest affected organ, is considered an early marker of disease activity in SSc [1]. The Modified Rodnan Skin Score (MRSS) is the standard skin assessment tool in the majority of clinical studies of SSc [2]. However, the MRSS is a palpation method, which is subjective and, thus, accuracy is user-dependent [3]. We have developed a noninvasive ultrasound surface wave elastography (USWE) technique for measuring skin elastic properties. The purpose of this paper is to demonstrate the clinical use of USWE for quantitative assessment of patients with SSc.

II. METHOD

Surface wave propagation on the skin can be analyzed as wave propagation in a semi-infinite tissue medium. The equation for wave propagation in an isotropic and elastic medium is [4]

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

where $\vec{u}$ is the displacement vector, ρ is the mass density, and λ and μ are, respectively, the Lamé coefficients of the medium.

Since soft tissues are generally incompressible and their Poisson's ratios are in a narrow region between 0.45 and 0.50, the surface wave speed can be related to the elastic modulus of tissue as [5] and [6],

$$c_s = \frac{1}{1.05}\sqrt{\frac{\mu}{\rho}}, \qquad (2)$$

where μ is the shear elasticity in Pascal and ρ is the mass density of the tissue in kg/m^3.

For soft tissue under low frequency harmonic excitation, the Voigt's model, which consists of a spring of elasticity μ_1 and a damper of viscosity μ_2 connected in parallel, has been proven to be effective in modeling the linear viscoelastic material [7, 8]. The dispersion curve of wave speed with the excitation frequency can be formulated by,

$$c_s = \frac{1}{1.05}\sqrt{\frac{2(\mu_1^2 + \omega^2 \mu_2^2)}{\rho(\mu_1 + \sqrt{\mu_1^2 + \omega^2 \mu_2^2})}} \,. \tag{3}$$

In USWE, a 0.1s harmonic vibration at a frequency is generated on the skin, and the resulting time response of the skin is measured using an ultrasound probe. Let $s_1(t)$ and $s_2(t)$ represent the displacement responses at two locations on the skin; the phase change of surface wave propagation over the two location can be calculated with a cross-spectrum method. The cross-spectrum $S(f)$ of two signals $s_1(t)$ and $s_2(t)$ is defined as [9],

$$S(f) = S_1^*(f) \cdot S_2(f) = \left| S_1(f) \cdot S_2(f) \right| \cdot e^{-j\Delta\varphi(f)}, \tag{4}$$

where $S_1(f)$ and $S_2(f)$ are the Fourier transforms of $s_1(t)$ and $s_2(t)$, respectively; * denotes the complex conjugate and $\Delta\phi(f)$ is the phase change between $s_1(t)$ and $s_2(t)$ over distance at frequency f.

The phase change of surface wave with distance is used to measure the surface wave speed,

$$c_s = 2\pi f \left| \Delta r / \Delta\phi \right|, \tag{5}$$

where Δr is the radial distance of two measuring locations, $\Delta\phi$ is the wave phase change over distance, and f is the frequency. The estimation of wave speed can be improved by using multiple phase change measurements over distance.

Human studies were approved by the Mayo Clinic Institutional Review Board (IRB). In a prospective clinical study on patients with SSc and ILD, we use USWE to measure skin viscoelastic properties of patients and healthy control subjects. Patients are enrolled in this research based on their clinical diagnoses. Healthy subjects are enrolled as control if they do not have any skin and lung diseases.

A subject is tested in a sitting position. The subject's skin is tested on the forearm and upper arm bilaterally. A low intensity 0.1 second harmonic vibration is generated on the skin of a subject using a handheld vibrator. The measurement of surface wave speed on the skin is independent of the amplitude of excitation. A small tissue motion in tens of µm is enough for sensitive ultrasound detection of the generated tissue motion. An ultrasound probe is aligned with the indenter of the vibrator to measure the generated surface wave propagation on the skin. To improve the imaging quality of skin, an ultrasound gel pad standoff Aquaflex® (Parker Laboratories, Inc., New Jersey 07004) is used. The surface wave speed of skin is measured at 100 Hz, 150 Hz, and 200 Hz. Three measurements are made at each location and each frequency.

III. RESULTS

Surface wave speed on the skin is measured by determining the change in wave phase with distance along the skin. Figure 1 shows representative B-mode images of the skin for a patient. The top dark area of the image shows the Aquaflex® standoff gel pad. The skin motion at eight locations is measured to calculate the surface wave speed of skin. The skin motion velocities at these locations are measured in the normal direction of skin using the ultrasound tracking beams through those locations [9, 10]. The skin motion is in response to the external vibration excitation induced by the handheld vibrator. A Verasonics ultrasound system (Verasonics, Inc., Kirkland, WA 98034) with a probe of L11-4 is used in this research. A high pulse repetition rate of 2000 frame/s is used to detect tissue motion in response to the excitations of 100, 150 and 200 Hz. Using the skin motion at the first location as a reference, the wave phase delay of the skin motion at the remaining locations, relative to the first location, is used to measure the surface wave speed. Figure 2 shows a representative wave speed at 100 Hz for the patient. The surface wave speed is 3.69 m/s for the patient. The wave speed on the skin is measured by analyzing ultrasound data directly from the skin. Therefore, the wave speed measurement is local and independent of the location and amplitude of excitation. Three measurements are made for each frequency and at each location.

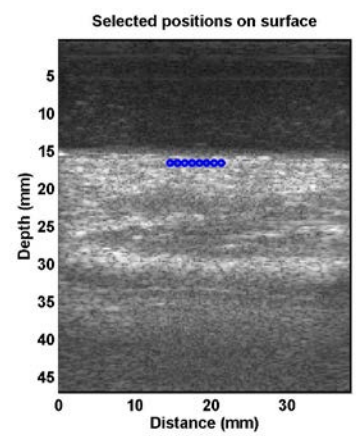

Figure 1. Representative B-mode image of skin for a patient. An ultrasound gel pad standoff is used to improve the imaging of skin. The top dark area in the imaging is associated with the gel pad. Eight locations on the skin surface are used to measure the surface wave speed of skin.

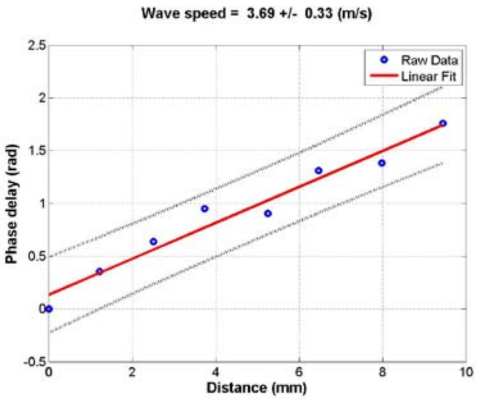

Figure 2. The wave phase delay of the remaining locations, relative to the first location, is used to measure the surface wave speed. Representative examples of wave speed at 100 Hz for a patient.

Significant differences in wave speed between healthy subjects and SSc patients were found. For example, the surface wave speed of the skin is 1.83 ± 0.04 m/s at 100 Hz, 2.33 ± 0.25 m/s at 150 Hz, and 3.04 ± 0.37 m/s at 200 Hz for a healthy subject, and the surface wave speed of the skin is 2.82 ± 0.31 m/s at 100 Hz, 3.60 ± 0.38 m/s at 150 Hz, and 5.36 ± 0.55 m/s at 200 Hz for an age matched SSc patient in the same location.

IV. Conclusion

USWE is a noninvasive technique for generating and measuring surface wave propagation on the skin. A subject’s skin is measured bilaterally on the forearm and upper arm. Significant differences of the surface wave speed between healthy subjects and patients were found. USWE can provide objective measurement of skin elastic properties in various regions of the body, which may be useful for quantitatively assessing patients with SSc.

Acknowledgment

This study is supported by NIH R01HL125234 from the National Heart, Lung, and Blood Institute.

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