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● *Original Contribution*

QUANTITATIVE ASSESSMENT OF SKIN STIFFNESS IN LOCALIZED SCLERODERMA USING ULTRASOUND SHEAR-WAVE ELASTOGRAPHY

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Abstract—The purpose of this study was to evaluate the usefulness of ultrasound shear-wave elastography (US-SWE) in characterization of localized scleroderma (LS), as well as in the disease staging. A total of 21 patients with 37 LS lesions were enrolled in this study. The pathologic stage (edema, sclerosis or atrophy) of the lesions was characterized by pathologic examination. The skin elastic modulus (E-values including E_{mean}, E_{min}, E_{max} and E_{sd}) and thickness (h) was evaluated both in LS lesions and site-matched unaffected skin (normal controls) using US-SWE. The relative difference of E-values (E_{RD}) was calculated between each pair of lesions and its normal control for comparison among different pathologic stages. Of the 37 LS lesions, 2 were in edema, 22 were in sclerosis and 13 were in atrophy. US-SWE results showed a significant increase of skin elastic modulus and thickness in all lesions ($p < 0.001$ in sclerosis and $p < 0.05$ in atrophy) compared with the normal controls. The measured skin elastic modulus and thickness were greater in sclerosis than in atrophy. However, once normalized by skin thickness, the atrophic lesions, which were on average thinner, appeared significantly stiffer than those of the sclerosis (normalized E_{RD}: an increase of 316.3% in atrophy vs. 50.6% in sclerosis compared with the controls, $p = 0.007$). These findings suggest that US-SWE allows for quantitative evaluation of the skin stiffness of LS lesions in different stages; however, the E-values directly provided by the US-SWE system alone do not distinguish between the stages, and the normalization by skin thickness is necessary. This non-invasive, real-time imaging technique is an ideal tool for assessing and monitoring LS disease severity and progression. (E-mail: wsqiuli@126.com)   © 2017 World Federation for Ultrasound in Medicine & Biology.

Key Words: Localized scleroderma, Ultrasound, Shear-wave elastography, Skin elasticity.

INTRODUCTION

Localized scleroderma (LS), also called *morphea*, is a term encompassing a spectrum of sclerotic autoimmune diseases that primarily affect the skin (Arkachaisri et al. 2010; Kreuter 2012). Localized and systemic scleroderma share the same histopathology features (Kreuter 2012). Because of these diseases the skin involvement can span from edema to sclerosis and eventually atrophy because of collagen overproduction and increased extracellular matrix deposition (Bendeck and Jacobe 2007; Kaloudi et al. 2010; Kreuter 2012; Weibel et al. 2007). These diseases are rare, and evidence-based treatment options of LS are limited because of the lack of the knowledge in pathologic causes and validated disease assessment methods (Bendeck and Jacobe

2007; Fett and Werth 2011; Li et al. 2011). An appropriate assessment of the diseases should be sensitive to change in the lesions (Bendeck and Jacobe 2007). Several methods for LS assessment are currently under investigation (Kreuter 2012).

No available laboratory markers in LS diagnosis have been approved (Li et al. 2010), although autoimmune phenomena (*e.g.,* antibodies and cytokines) have been reported frequently in LS patients (Kreuter 2012). The localized scleroderma assessment tool is a promising tool for clinical skin scoring because it differentiates between activity and damage, can identify change and requires no additional equipment (Arkachaisri et al. 2010; Fett and Werth 2011). However, the localized scleroderma assessment tool still seems controversial and appears to be complicated and time-consuming (Wortsman et al. 2011). Moreover, the deeper lesions of LS may progress before clinical signs become apparent (Li et al. 2011). Among instrumental methods, laser Doppler flowmetry can be used to discriminate disease

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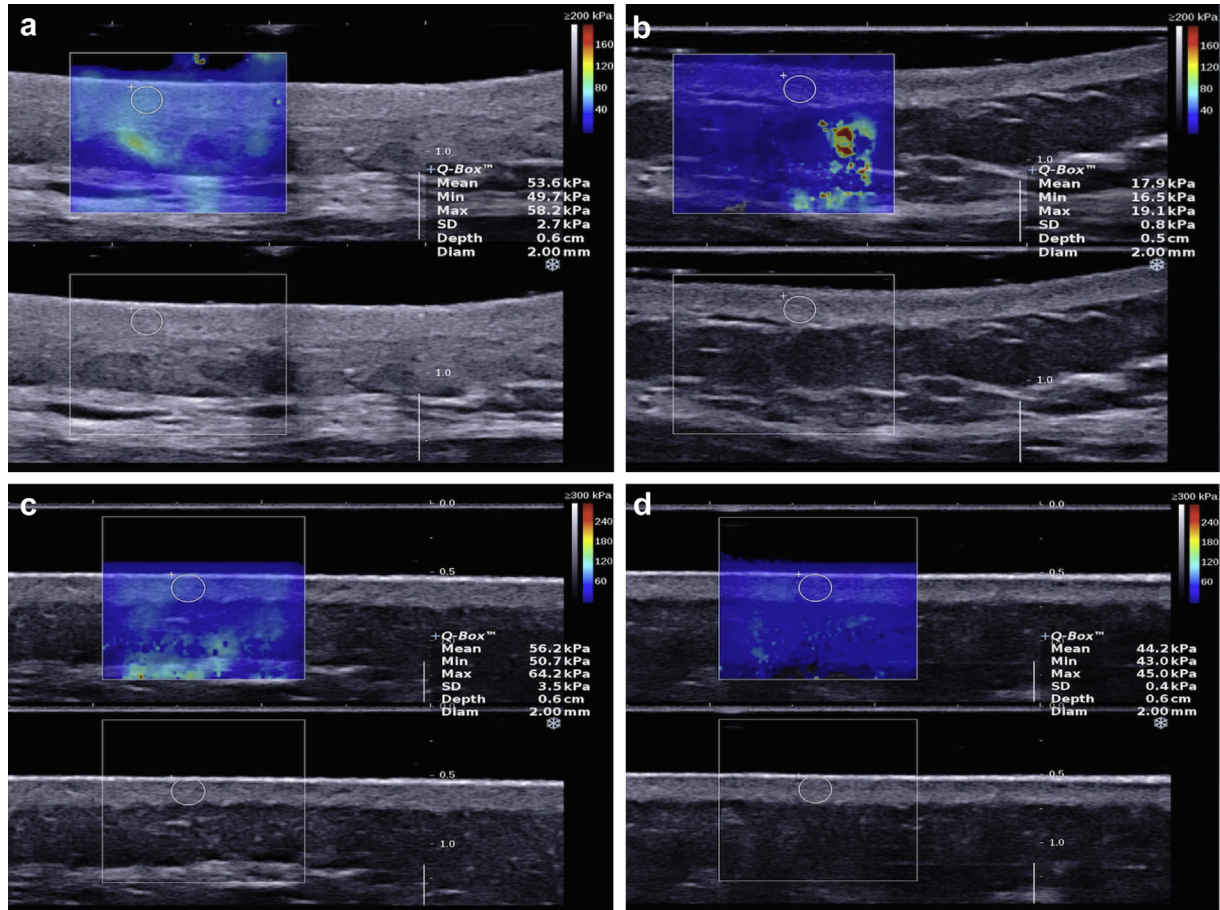
Fig. 1. US-SWE images of LS lesions. The SWE box (upper picture) was superimposed to the B-mode image (lower picture) to adequately depict the epidermis, dermis and subcutis. The skin thickness (including epidermis and dermis) was measured in the B-mode image. The quantitative skin elastic moduli including mean, minimum, maximum and standard deviation were automatically calculated by the US system and displayed in the picture. (a) and (c) are US-SWE images of LS lesions at sclerosis and atrophy, respectively. (b) and (d) are US-SWE images of their corresponding normal controls. LS = localized scleroderma; US-SWE = ultrasound shear-wave elastography.

activity in LS patients (Weibel et al. 2007) but fails to provide morphologic information (Wortsman et al. 2011). Thermography—the recording of differences in skin surface temperature between affected and normal areas—requires a temperature-controlled room (Wortsman et al. 2011), and there is a risk of false-positive results in atrophic lesions (Martini et al. 2002; Weibel et al. 2007). Zulian and Martini (2007) introduced a computerized skin score for accurately assessing the skin lesions of LS. A limitation of the computerized skin score might be low sensitivity to change, because LS lesions do not shrink as they resolve (Fett and Werth 2011). Magnetic resonance imaging and computed tomography might be useful to detect potential involvement of the central nervous system, muscle or bone, but these techniques have limited availability and a high cost, and they provide poor resolution for the dermal layer (Kreuter 2012; Wortsman et al. 2011). High-frequency ultrasound

scanning has been used for the detection of skin thickness and echogenicity in LS (Bendeck and Jacobe 2007; Cosnes et al. 2003; Li et al. 2011; Nezafati et al. 2011), and both of those parameters could assist in differentiation between disease stages (edema, sclerosis and atrophy) (Nezafati et al. 2011).

Skin sclerosis, the hallmark feature of LS, greatly affects the skin elasticity (Kreuter 2012). However, none of the methods mentioned earlier can directly assess skin elasticity. Elastography, which allows assessment of tissue elastic properties and provides a novel method to quantitatively evaluate tissue stiffness, can be performed using two major modalities: strain elastography (SE) and shear-wave elastography (SWE) (Inoue and Kokudo 2014). SE measures the degree of deformation of the subject and converts the extent of deformation inside the region of interest (ROI) into a specific color (Arda et al. 2011; Hou et al. 2015; Inoue and Kokudo 2014; Ophir