

### 1 Background

Skin involvement is of major clinical and prognostic relevance in systemic sclerosis (SSc) and is often the primary outcome of clinical trials in SSc. Nevertheless, a fully validated, objective and sensitive measure of skin involvement is lacking.

Shear-wave elastography in the form of Siemens' proprietary, Virtual Touch and Imaging Quantification (VTIQ), is an emerging, operator-independent technique, which can obtain absolute quantitative stiffness values.

The objective of this study was to determine validity and reliability of shear-wave elastography for measuring skin stiffness as a measure of skin involvement in SSc.

### 2 Methods

#### ➤ Patients

26 consenting patient with confirmed SSc (2013 classification criteria) underwent clinical evaluation and demographic data collection. 17 age and gender-matched healthy volunteers were recruited from the hospital staff and patients' family members.

#### ➤ Modified Rodnan skin score (mRSS)

Skin thickness was clinical assessed over 17 anatomical anatomical sites

#### ➤ Ultrasound evaluation

Absolute skin stiffness (shear wave velocity, in m/s) was measured at all mRSS anatomical sites (except face)

Siemens ACUSON S3000™ ultrasound system with a linear 4-9MHz transducer. Sampling gates sized 2x2mm.

Higher shear-wave velocity value indicates higher tissue stiffness.

#### ➤ Reliability

Intra-observer reliability was assessed by intraclass correlation coefficients (ICC) in 4 SSc patients at all 17 sites and 2 healthy controls, in 2 sequential scanning sessions, one week apart.

#### ➤ Statistical analysis

Correlations between absolute skin stiffness and mRSS, and comparison between patients and controls were statistically performed using a two-tailed t-test, in SPSS software. P values <0.05 were considered significant.

### 3 Results

**Table 1 - Clinical features of SSc patients and controls.**

➤ The study included 26 SSc (13 diffuse 13 limited subset) and 17 age-matched controls

	SSc patients	Controls
Gender (F/M)	23/3	14/3
Age, mean (SD) (years)	55.3 (12.1)	54.3±14.8
Disease duration from RP, mean (SD) (years)	14.9 (9.4)	-
Disease duration from diagnosis, mean (SD) (years)	12.5 (8.7)	-
Disease subset (D/L)	13/13	-
ANA, n (%)	26 (100.0)	-
ACA, n (%)	9 (34.6)	-
Antitopoisomerase I, n (%)	10 (38.5)	-
Anti-PMScI, n (%)	2 (7.7)	-
mRSS, mean (SD)/range	11.8 (9.2)/0-33	-

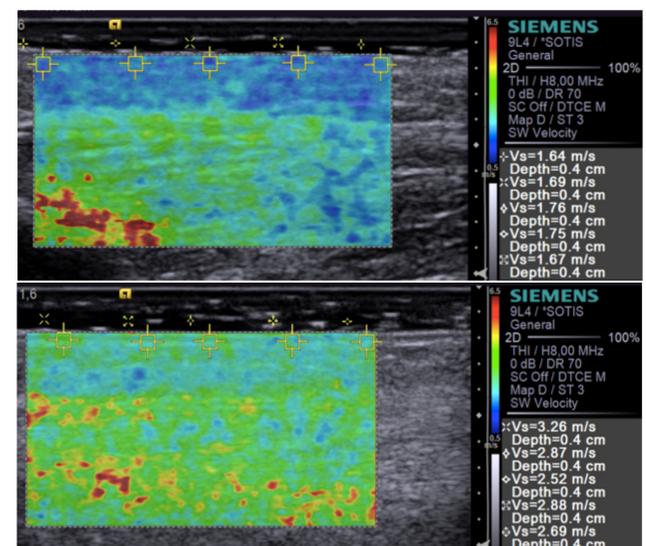
ACA, anticentromere antibodies; ANA, antinuclear antibodies; D, diffuse cutaneous SSc; L, limited cutaneous SSc; mRSS, modified Rodnan skin score; RP, Raynaud's Phenomenon.

➤ Absolute skin stiffness measurements were statistically significantly higher in SSc than in controls, in 6 out of 9 mRSS anatomical sites of analysis (table 2).

➤ The ICCs for agreement between ultrasound measurements was 0.8.

**Table 2- mRSS and shear-wave velocity values (m/s) in SSc patients and controls.**

Rodnan sites	mRSS at the site of analysis, mean (SD)/range	Nr of SSc cases with mRSS=0, at the site	Shear-wave velocity values		Patients vs. Controls (p value)
			SSc patients (n=26), mean (SD)	Controls (n=17), mean (SD)	
Anterior chest	0.5 (0.7)/0-2	17	2.7 (1.1)	2.3 (0.7)	0.15
Abdomen	0.2 (0.5)/0-2	21	2.4 (0.8)	2.2 (0.3)	0.06
Upperarm	0.4(0.6)/0-2	18	2.9 (1.0)	2.2 (0.2)	<b>0.001</b>
Forearm	0.9 (0.7)/0-2	13	3.1 (1.1)	2.2 (0.3)	<b>0.001</b>
Hand	1.1 (0.9)/0-3	7	4.0 (1.5)	2.2 (0.3)	<b>0.001</b>
Phalanx	1.8(0.9)/0-3	2	4.3 (2.0)	2.2 (0.2)	<b>0.001</b>
Thigh	0.1(0.3)/0-1	23	2.6 (0.4)	2.1 (0.2)	<b>0.001</b>
Leg	0.4 (0.6)/0-2	19	3.1 (0.9)	2.4 (0.4)	<b>0.001</b>
Foot	0.6(0.8)/0-3	14	3.2 (0.9)	2.3 (0.2)	0.01



A - Control

B - Patient

Shear-wave elastography of the dorsal aspect of the hand. Absolute shear-wave velocities (in m/s) within the sample gate (yellow box) are shown quantitatively on the right side. The color scale depicts graphically the absolute stiffness of all tissues within the region of interest. (red=hard tissue; blue=soft tissue).

### 4 Discussion

We found systematically higher absolute skin stiffness values in SSc patients than controls.

Possible implications of shear-wave elastography:

- May represent a valuable tool in quantitative assessment of skin involvement in SSc
- May differentiate subclinical skin changes, ie corresponding to an mRSS of zero

Further studies are required, but this early study supports the clinical and scientific potential of this new measure of skin involvement in SSc.

### 5 Conclusions

- Shear-wave elastography represents a feasible and reproducible quantitative method for assessing stiffness in scleroderma skin
- Shear-wave elastography is an innovative and promising technique that provides, for the first time, a non-invasive, absolute quantification of tissue stiffness.
- Further studies are needed in larger cohorts of patients with varying degrees of skin thickening, and in longitudinal studies.