

SHEAR-WAVE ELASTOGRAPHY:

Is it possible to distinguish “unaffected” skin in scleroderma patients from healthy skin?

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Introduction

- **Skin involvement is of major clinical and prognostic relevance in systemic sclerosis (SSc)**
- **Often the primary outcome in clinical trials in SSc**
- **Modified Rodnan Skin Score (mRSS)**
 - Semi-quantitative measure of cutaneous involvement assessed by palpation
- **However, the mRSS has been criticized for:**
 - High intra- inter-observer variability (12% and 25%, respectively)
 - Dependent on training and experience
 - Cannot differentiate between three phases of the disease

A fully validated, objective and sensitive measure of skin involvement is lacking.

Shear-wave elastography

- **Elastography** is a new ultrasound-based imaging modality that has aroused the interest of researchers in ultrasound imaging technology during the last two decades:
 - **Compression elastography**
 - **Shear-wave elastography**
- **Shear-wave elastography** provides quantitative measurements of tissue stiffness by measuring the velocity of propagation of a shear-wave in tissues
 - **Virtual Touch Imaging and Quantification (VTIQ)**
 - ✓ (More) operator independent
 - ✓ Absolute values
 - ✓ Allows the use of small adjustable sampling gates in order to assess discrete anatomical structures

We hypothesize that VTIQ may provide a non-invasive sensitive means for absolute quantification of skin stiffness, which may have considerable impact upon clinical practice and research in SSc.

Objective

- To compare absolute skin stiffness values of ***clinically unaffected scleroderma skin*** and the **skin of *healthy controls***, using **shear-wave elastography**.

Methods

- **Participants**

- 26 SSc patients
- 17 HC (age- and gender-matched)

- **Rodnan skin score**

- Skin thickness measured over 17 anatomical sites

- **Ultrasound evaluation**

- Absolute skin stiffness (shear-wave velocity, (in m/s) was measured at all mRSS anatomical sites
- Siemens ACUSON S3000™ ultrasound system with a linear 4-9MHz transducer. Sampling gates sized 2x2mm.

- **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**

- SPSS version 20.0. Mann-Whitney test was used to evaluate differences between groups. P value <0.05 were considered significant.

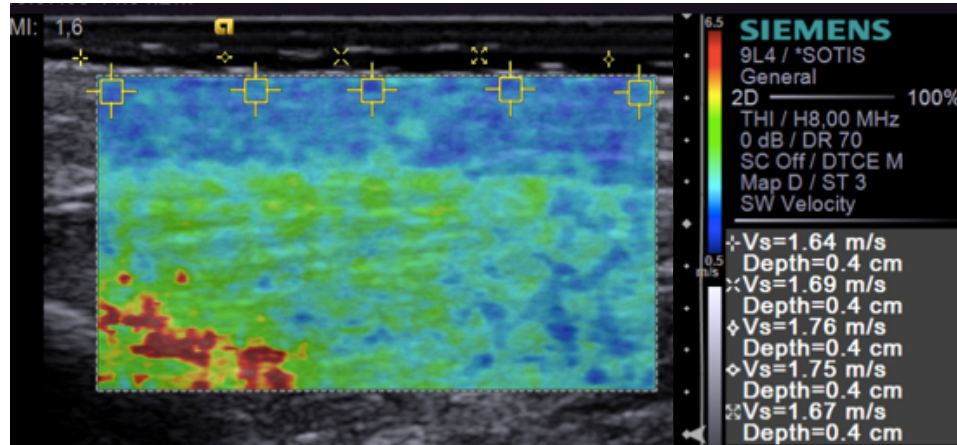
Results (I)

	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 (%)	10 (38.5)	
Anti-topoisomerase I, n (%)	9 (34.6)	
Anti-PMScl, n (%)	2 (7.7)	
mRSS, mean (SD)/range	11.8 (9.2)/0–33	

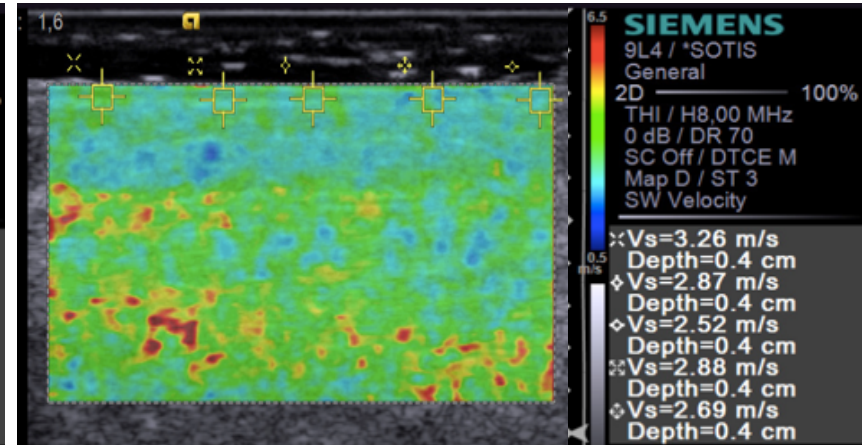
ACA, Anticentromere antibodies; ANA, Antinuclear antibodies; D, Diffuse cutaneous SSc; L, Limited cutaneous SSc; RP, Raynaud's Phenomenon.

Results (II)

Shear-wave elastography of the dorsal aspect of the hand.



(A) Healthy Control



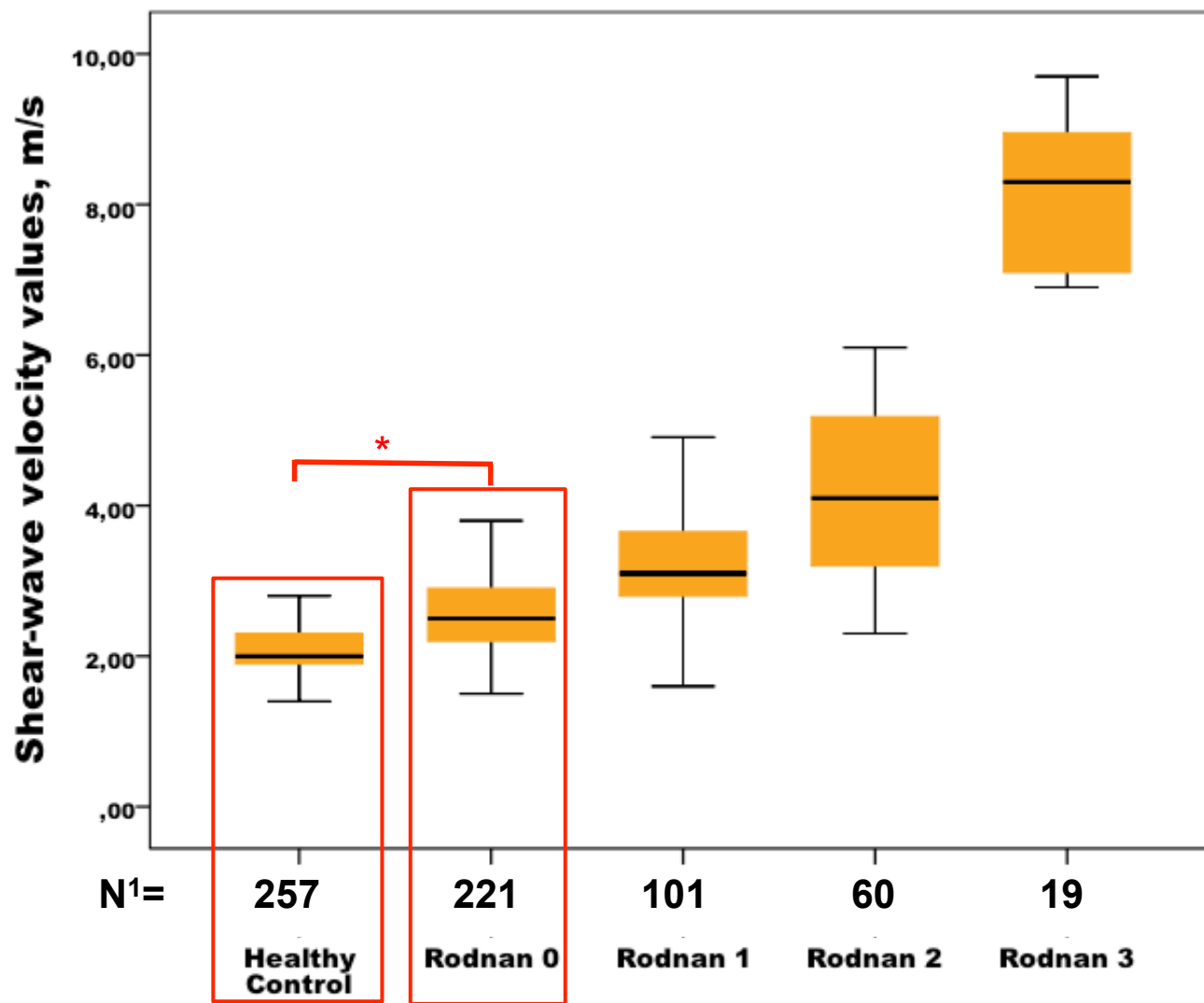
(B) Patient

Results (III) – Shear wave velocities values (m/s) in unaffected skin from SSc patients vs. Controls

	SSc patients n= 26 (*)	Controls n= 17	<i>P</i>
Anterior chest	2.8±0.7 (17)	2.3±0.7	NS
Abdómen	2.5±0.4 (21)	2.1±0.4	0.024
Upperarm	2.4±0.4 (19)	2.2±0.3	NS
Forearm	2.6±0.3 (14)	2.1±0.3	0.053
Hand	2.6±0.6 (7)	2.2±0.3	NS
Phalanx	2.9±0.3 (3)	2.1±0.2	0.006
Thigh	2.4±0.4 (18)	2.1±0.2	0.002
Leg	2.4±0.6 (18)	2.3±0.3	NS
Foot	2.8±0.6 (14)	2.3±0.3	0.004

*Number of patients with mRSS = 0 at each site.

Results (IV) – Shear-wave velocity values according to clinical skin score.



¹Total number of skin sites with this clinical classification.* = $P < 0.05$, ** = $P < 0.01$

Discussion

- Our results indicate that shear-wave elastography is capable of identifying **significantly increased stiffness in skin from SSc patients as measured in sites considered clinically 'unaffected'**.
- This study provides the **first quantitative and objective measurement** of absolute skin stiffness in SSc.
- This is in agreement with recent microarray gene expression studies suggesting that clinically unaffected skin shares the peculiar gene signatures and the pathology of clinically affected skin in SSc [Frost J, et al 2012; Pendergrass SA 2012, Milano, 2008]
- This increased sensitivity of shear-wave elastography in the **early stages of skin involvement** may represent a valuable contribution to clinical assessment and especially, to research in the pathogenesis and treatment of this disease.

Conclusion

- These findings strongly supports that **shear-wave elastography** represents valuable progress in the quantitative assessment of skin stiffness.
- It adds sensitivity and precision to the **non-invasive assessment of skin involvement in SSc**, which may be decisive in the evaluation of new interventions.
- **Longitudinal studies** in a large number of patients, with multiple independent observers, are needed to assess inter-observer reliability and sensitivity to change over time.
- Such studies, together with technical improvements in the methodology, may well establish VTIQ as a **valuable quantitative outcome measure for clinical and research work in SSc**.

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Obrigado pela atenção.