

VIRTUAL TOUCH IMAGING AND QUANTIFICATION: A NEW NON-INVASIVE IMAGING METHOD TO MEASURE SKIN STIFFNESS FOR SCLERODERMA

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1 Background

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

Virtual Touch Imaging and Quantification (VTIQ) is a new elastography imaging method that provides qualitative and quantitative information about absolute skin stiffness.

The objective of this study was to evaluate VTIQ as a potentially method for determining absolute skin stiffness in SSc.

2 Methods

Patients

26 consenting patient with confirmed SSc (2013 classification criteria for SSc) underwent clinical and demographic data collection.

17 age and gender-matched healthy volunteers were recruited from hospital staff's and patients' family members.

Rodnan skin score (mRSS)

➤ Skin thickness measured over 17 anatomical anatomical sites

Ultrasound evaluation

➤ Absolute skin stiffness (shear wave velocity, (in m/s) was measured at all mRSS anatomical sites using a Siemens ACUSON S3000™ ultrasound system with a linear 4-9MHz transducer. Sampling gates sized 2x2mm. A greater 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-tests, in SPSS software. P values <0.05 were considered significant.

3 Results

➤ 13 SSc patients with diffuse and 13 with limited subset were enrolled. The mean age of SSc patients and controls was not statistically different ($p > 0.05$) (table 1).

Table 1 - Clinical features of SSc patients and 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+	26 (100.0%)	-
ACA+	9 (34.6%)	-
Antitopoisomerase I+	10 (38.5%)	-
Anti-PMScI	2 (7.7%)	-
mRSS, mean (SD)/range	11.8 (9.2)/0-33	-

Table 2- Clinical features 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)	NS
Abdomen	0.2 (0.5)/0-2	21	2.4 (0.8)	2.0 (0.4)	NS
Upperarm right	0.4 (0.6)/0-2	19	2.5 (1.1)	2.2 (0.5)	NS
Upperarm left	0.3 (0.6)/0-2	18	2.9 (1.2)	2.3 (0.4)	0.03
Forearm right	0.7 (0.7)/0-2	13	3.1 (1.2)	2.3 (0.3)	0.005
Forearm left	1.1 (0.9)/0-3	14	2.9 (0.9)	2.1 (0.4)	0.001
Hand right	1.1 (0.9)/0-3	7	4.3 (2.4)	2.2 (0.4)	0.0001
Hand left	1.1 (0.9)/0-3	7	3.6 (1.8)	2.2 (0.5)	0.001
Phalanx right	1.8 (0.9)/0-3	3	4.2 (2.2)	2.2 (0.3)	0.0001
Phalanx left	1.7 (1.0)/0-3	1	4.4 (2.1)	2.3 (0.4)	0.0001
Thigh right	0.1 (0.3)/0-1	23	2.4 (0.8)	2.1 (0.2)	0.02
Thigh left	0.1 (0.3)/0-1	23	2.4 (0.6)	2.1 (0.3)	0.03
Leg right	0.4 (0.6)/0-2	18	2.9 (1.2)	2.4 (0.6)	NS
Leg left	0.4 (0.6)/0-2	19	2.9 (1.3)	2.3 (0.4)	0.04
Foot right	0.6 (0.8)/0-3	15	3.3 (1.4)	2.2 (0.3)	0.006
Foot left	0.6 (0.8)/0-3	14	2.7 (1.1)	2.3 (0.4)	NS

➤ Absolute skin stiffness measurements were statistically significantly higher in SSc than in HC, in 11 out of 16 mRSS sites of analysis (table 2).

Shear-wave velocity values and local mRSS

➤ Absolute skin stiffness was strongly correlated with the local mRSS in the following anatomical sites: forearm, $r = 0.688$, $p = 0.0001$; hand, $r = 0.577$, $p = 0.0001$; and, phalanx, $r = 0.748$, $p = 0.0001$

➤ The ICCs for agreement between ultrasound measurements was 0.8.

4 Discussion

We found systematically and significantly higher absolute skin stiffness values in SSc patients than controls, in 11 out of 16 mRSS sites.

Possible implications:

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

Absolute skin stiffness values were strongly correlated with the local mRSS in the forearm, hand and finger.

Possible reasons:

- Lack of correlations in other sites may be due the low scores and low range of mRSS in those sites.
- VTIQ and skin score do not measure exactly the same properties of the skin. The mRSS measures not only thickness, but also texture and fixation, while VTIQ measures the stiffness of the skin. This differences will need to be taken into account in future when further addressing correlations between the two methods.

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

5 Conclusions

- VTIQ of the skin could offer a feasible and reliable quantitative outcome measure for skin involvement in SSc.
- Shear wave velocities showed a strong positive correlation with mRSS in at least three sites.
- VTIQ represents an innovative and promising technique that provides, for the first time, a non-invasive, absolute quantification of tissue stiffness.
- VTIQ now needs to be applied in larger cohorts of patients with varying degrees of skin thickening, and in longitudinal studies.