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A Quantitative Description of Echographic Images of Sclerotic Skin in Patients with Systemic Sclerosis, as Assessed by Computerized Image Analysis on 20 MHz B-scan Recordings

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The aim of our study was to find image descriptors enabling the characterization of sclerotic skin and its differentiation from normal skin, in order to find an objective method for the assessment of skin involvement in systemic sclerosis (SSc). Echographic evaluations were carried out using a 20 MHz B-scanner, on 18 female patients with SSc and on 20 healthy women serving as controls, at 3 different skin sites (forehead, cheek and back of the hand). Images were processed by a program, based on segmentation procedures and object description, employing 5 different amplitude bands and the following parameters: 1) the extension of image areas marked by amplitude bands of interest, 2) the percentage of the image surface reflecting within a homogeneous amplitude band, 3) the number of objects composing the image, 4) the average object size, and 5) the "density" of the objects.

At all 3 skin sites, marked differences in the echostructure of the tissue between patients with SSc and the controls were observable. In SSc patients forehead skin appeared thinner and more echogenic, with smaller hypo-reflecting objects and greater hyper-reflecting areas; cheek skin showed an increase in intermediate-high amplitude components, with greater and more numerous hyper-reflecting objects, and smaller and less numerous hypo-reflecting ones; the skin on the back of the hand was thicker, less echogenic, with large hypo-reflecting areas and small hyper-reflecting objects. By image processing these parameters were numerically described. Values referring to sclerotic skin significantly differed from those of normal skin. This echographic procedure is proposed as a method representing a first step towards the quantification of the spontaneous course of SSc and of response to therapy. *Key-words: scleroderma; ultrasound; image processing.*

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Systemic sclerosis (SSc) is a systemic connective tissue disease, associated with modifications of the skin and characterized by an increased mass of collagen fibers in the papillary and reticular dermis, with atrophy of the normal dermal appendages. Clinically, 3 phases of skin involvement can be identified: an early oedematous phase, an indurative phase, and an atrophic phase in which thinning of the abnormal skin occurs (1, 2). The degree of cutaneous involvement together with changes in skin thickness seem to correlate with the disease severity (3–5).

Besides the determination of the weight of a forearm skin biopsy (6), the total skin score (5) and xeroradiographic techniques assessing skin thickness (7, 8), non-invasive skin thickness determination by A- and B-scanning methods has been employed to determine the degree and the extent of the skin involvement in SSc patients: skin thickness, determined on the extensor and flexor aspects of the forearms (9, 10), on the middle and proximal phalanges (9, 11) and on the chest (12), was found to have increased in a variable percentage of patients.

New approaches to non-invasive estimation of the skin structure have been provided by recent advances in ultrasound technology. As a digitalized image, an echographic picture is a visual representation of arrays of numbers, each picture element representing the amount of reflected ultrasound. Image processing procedures achieve the numerical representation of the image and the quantification of the echographic data, enabling their statistical elaboration (13). Processing of B-scan images allows the characterization of site-, sex-, and age-dependent variations in normal skin (14), and the description of changes associated with inflammatory disorders, like skin sclerosis in plaque-type scleroderma (15), by means of segmentation procedures and object description.

The aim of our study was to find image descriptors enabling the characterization of sclerotic skin of patients with SSc and its differentiation from normal skin, using processing methods for elaborating 20 MHz B-scan images, to find an objective method for the assessment of skin involvement in SSc.

MATERIALS AND METHODS

Patient population

Eighteen female patients who met the American Rheumatism Association criteria for the classification of SSc (16) were studied. The patients had diffuse cutaneous involvement and a different degree of organ involvement. Their age ranged from 31 to 80 years (average 56 ± 12) and the duration of the disease was from 2 to 25 years (average 10 ± 8). Fourteen patients received or had received medical treatment with Factor XIII, 7 with penicillamine, 6 with corticosteroids.

Twenty healthy age-matched women were studied for control purposes.

Images were recorded on 3 different skin sites: the middle of the forehead, the right cheek, and the back of the right hand.

Ultrasound equipment

Echographic evaluations were carried out using a 20 MHz B-scanner (Dermascan C, Cortex Technology, Denmark), which produces images representing a cross section of the skin. Equipment, calibration methods and recording conditions have already been described in detail elsewhere (17). Evaluations were performed by employing the B-probe assessing a 12.13-mm-long tissue section. At skin sites where the dermis-hypodermis boundary was difficult to determine, owing to a low echogenicity of the dermis, images were recorded both with an increased time-gain compensation, for skin thickness measurements, and with a constant gain, enabling image processing.

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Software for image analysis

The echographic images were processed by a software (Dermavision 2D, Cortex Technology), based on segmentation procedures and object description (15). Evaluations were performed by means of amplitude bands, marking the hypo-reflecting parts of the dermis (0–10 and 0–30), and by intervals identifying intermediate echo-amplitudes (31–75 and 76–126). A 127–255 band was used for evaluating hyper-reflecting dermal structures. As a region of interest the whole skin block appearing on the screen without the entrance echo was chosen.

For characterizing sclerotic skin, the following parameters were considered for different amplitude intervals: 1) the extension of image areas marked by amplitude bands of interest (in number of pixels), 2) the percentage of the image surface defined by a region of interest reflecting within a homogeneous amplitude band, 3) the number of objects composing the image, 4) the average object size, obtained by dividing the extension of homogeneous amplitude areas by the number of objects, and 5) the "density" of the objects, obtained by referring the number of objects to the thickness of the skin (expressed in mm).

The first parameters described the area in the picture marked by a certain amplitude level; the number of objects and their size describe the distribution of certain amplitude bands, whereby a small number of large objects corresponds to a relatively homogeneous picture with large or confluent image areas, while a few, small objects are characteristic of a picture consisting of little spots with an unhomogeneous distribution. By referring the number of objects to skin thickness, information about the distance between the different objects can be obtained.

Statistics

Differences in the echographic parameters between sclerotic and normal skin were analyzed by Student's *t*-test for unpaired data. Correlations between skin thickness values and duration of the disease were calculated according to Pearson. Probabilities less than 0.05 were considered significant.

RESULTS

The distribution of the echogenicity of sclerotic skin varies in respect to the skin of healthy subjects. At the forehead and cheek the definition of the dermis-hypodermis boundary is difficult, when wide highly reflective projections extend into the subcutaneous tissue in a direction sometimes parallel to the skin surface, so as to simulate a double hyper-reflecting lower dermal band, and at times, oblique in respect to it.

Fig. 1 represents the echographic aspect of sclerotic skin of the forehead and the cheek in comparison to normal skin.

Skin thickness

The results of skin thickness measurements in mm appear in Table I (mean ± s.d.). In SSc patients, skin thickness values were significantly higher on the back of the hand, whereas at forehead and cheek a significant thinning was observable. In 12 SSc patients and 15 healthy subjects it was possible to determine the epidermis-bone thickness on the forehead. Values were 3.99 ± 0.88 for SSc patients and 4.24 ± 0.80 for healthy subjects. The difference is not significant. No correlation was present between skin thickness and duration of the disease.

Figs. 2 and 3 illustrate the results of the elaboration of images referring to forehead, right cheek and back of the right hand.

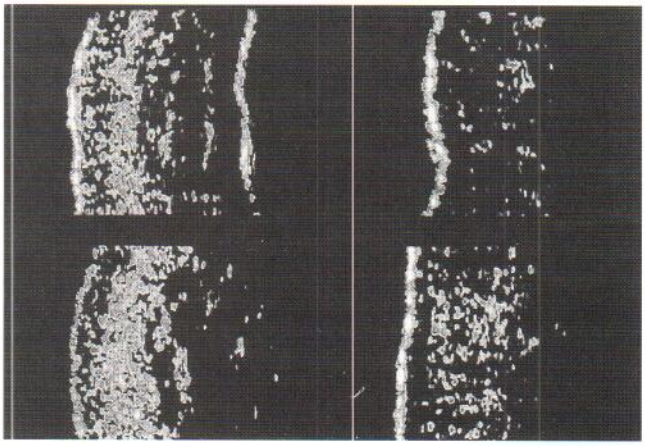

Fig. 1. Echographic images of normal skin (on the right) and of sclerotic skin (on the left): in these images the whole amplitude scale is represented; high amplitude values correspond to white, low amplitude values to black. The entrance echo, referring to the epidermis, appears as a white band; black areas in the right part of the pictures represent the subcutaneous fatty tissue. *Upper left corner*: forehead skin in a PSS patient; *upper right corner*: forehead skin in an healthy subject; *lower left corner*: cheek skin in an SSc patient; *lower right corner*: forehead skin in a healthy subject.

Table I. *Skin thickness values in mm (mean ± s.d.) in 18 patients with progressive systemic sclerosis and 20 control subjects*

Area	Forehead	Right cheek	Back of the right hand
PSS	1.56 ± 0.20*	1.62 ± 0.33*	1.51 ± 0.41*
Healthy subjects	1.85 ± 0.27	1.86 ± 0.24	1.17 ± 0.18

* significant in respect to healthy subjects.

Forehead

In SSc patients absolute and relative (Fig. 2) extensions of image areas referring to 0–10 and 0–30 pixels were significantly lower, whereas 31–126 amplitude areas were more extended. The number of 31–75 objects was significantly inferior. The size of 0–10 objects had diminished, while that of 76–126 objects had increased (data not shown). Thus, on the whole, forehead skin appeared more echogenic, reflecting mainly within intermediate amplitude intervals. Hypo-reflecting areas were more extended and were subdivided into smaller areas.

Cheek

Echogenicity was higher in SSc patients: absolute and relative (Fig. 2) extensions of 109–255 areas were significantly higher. Hypo-reflecting areas were smaller and fewer, whereas hyper-reflecting objects were greater in size (data not shown).

Back of the right hand (Fig. 3)

On the whole, the skin appeared less echogenic, since the extension of hypo-reflecting (0–10 and 0–30) areas was higher in respect to healthy subjects. Moreover, significant differences

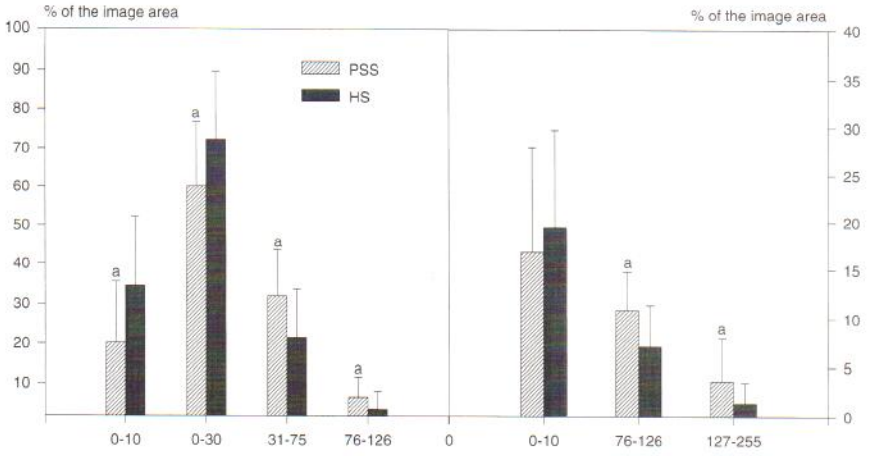

Fig. 2. Elaboration of echographic images after segmentation: % of image areas covered by homogeneous amplitude values. On the left, values referring to forehead skin, on the right, values referring to cheek skin. *a* = significant in respect to healthy subjects.

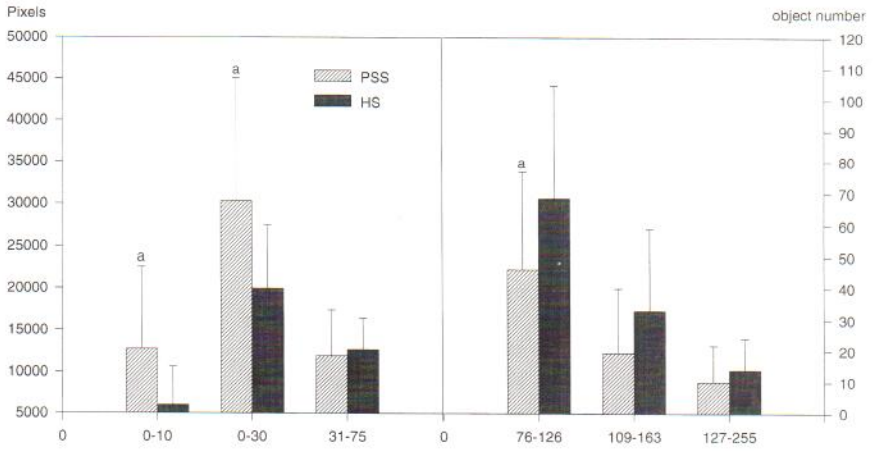

Fig. 3. Elaboration of echographic images of the skin of the back of the hand after segmentation and binary transformation. On the left, extension of homogeneous areas expressed in number of pixels referring to different amplitude intervals; on the right, the number of objects reflecting within homogeneous amplitude values. *a* = significant in respect to healthy subjects.

in respect to healthy subjects were observable for the number of 76–126 objects. For density values (object number/skin thickness ratio) significant differences were observed for the skin of the cheek using 127–255 segmentation (for SSc and healthy subjects 1.14 ± 0.81 and 0.64 ± 0.67, respectively) and for the back of the hand using the 76–126 interval (2.80 ± 2.22 and 4.98 ± 2.76, respectively).

DISCUSSION

Echographic examination represents a non-invasive procedure enabling reproducible and reliable measurements of skin thickness. Sclerotic skin thickness has been investigated by ultrasound both in morphoea and in patients with SSc (9–12, 15, 18–20). Serup (9) described increased skin-phalanx distance over the middle phalanx in most subjects affected by acrosclerosis. Åkesson et al. (11) observed that all patients with widespread scleroderma of short duration had significantly increased skin thickness on the dorsal aspect of the proximal and middle phalanges compared with controls. Investigating the skin on the chest, the forearm and the hand in SSc patients and healthy controls, Ihn et al. (12) demonstrated that also at clinically uninvolved skin sites a thickening is present in the former group. Although no correlation was found between skin thickness and duration of the disease, the thickening tended to be greater in patients with diffuse disease of recent onset (12). No data are available on skin thickness values on the back of the hand and on the face. Our measurements have evidenced a thickening on the back of the hand and, contrary to what is appreciated by palpation, a thinning on the forehead and the cheek. In fact, the echolucent area underlying the dermis, corresponding to the superior subcutaneous tissue, which is visible in healthy subjects, is not present or is thinner in most echographic images of the forehead and the cheek, and the dermis seems to adhere to the underlying layers; this corresponds to the impression of thickening and resistance to traction, which can be felt in SSc patients by lifting the skin with the fingers.

It is not certain that the interface between the echo-dense zone and the echo-poor more profound tissues really represents the dermis/subcutis border, as a basis for skin thickness measurement; in fact, there might be different alterations of the superficial and deep connective tissue giving rise to echo-dense modifications of the outer and echo-poor fibrosis of the lower part of the dermis. Yet, on the forehead, when the bone echo is assessable, the measurement of the skin surface/frontal bone surface distance confirms the reduction assessed by measuring the epidermis-dermis/subcutis interface distance.

So far, sclerotic skin of SSc patients has not been investigated by means of B-scanning echography associated with image analysis procedures. This method has already proved useful in the assessment of site-, age- and sex-dependent variations in normal subjects (14) and in the quantification of psoriasis (21) and of allergic and irritant patch test reactions (17, 22,

23). By elaborating echographic images of morphoea plaques, after segmentation with low-reflecting amplitude intervals, and comparing them to those referring to healthy contralateral or perilesional skin, sclerotic skin appeared comparatively homogeneous with few, large objects within a thickened skin block (15).

When observing the echographic image of sclerotic skin in SSc patients, one immediately notices great variations in respect to healthy skin pictures. On the forehead and the cheek, the subcutaneous tissue presents multiple hyper-reflecting bands parallel to the skin surface, adjacent to the dermis (Fig. 1), whereas on the back of the hand the skin seems considerably thicker and low-reflecting.

Numerical data referring to segmentation and object description of SSc patients' images show modifications which vary according to the skin site examined: in respect to healthy subjects, forehead skin is more echogenic, with hypo-reflecting objects, which are less extended and subdivided into smaller areas; cheek skin shows an increase in 127–255 components, with smaller and fewer hypo-reflecting areas and greater hyper-reflecting objects; finally, the skin of the back of the hand is less echogenic, with large hypo-reflecting areas and small hyper-reflecting objects, closely resembling the image of a morphoea plaque.

SSc is a chronic disease, undergoing spontaneous fluctuations with a tendency towards progressive worsening. Many therapeutic agents have been proposed, which are routinely employed without an adequate control of their efficacy. For longitudinal studies of disease progression or for the evaluation of treatment effectiveness, a painless noninvasive technique for determining skin changes in SSc is required. Ultrasound seems to offer a feasible, clinically useful alternative to subjective evaluation of SSc, since it provides objective parameters for the characterization and numerical description of sclerotic skin and for its differention from normal skin, as a first step towards quantification of the spontaneous course of the disease and of response to therapy.

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