Real-time spatial compound ultrasound imaging of skin

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Purpose: The aim of our study was to evaluate the potential of real-time spatial compound imaging (RTSCI) in dermatology.

Materials and methods: An ATL 5000 SonoCT equipped with compact linear 15–7 MHz and linear 12–5 MHz transducers was obtained for skin visualization in a group of dermatological patients with various skin diseases.

Results: Thirty-four people participated: 21 patients with various skin diseases and 13 persons with normal skin. The mean age was 43.4 years. For many diseases, RTSCI gave useful information about the lesional structure, thickness and relationship with surrounding structures.

Conclusion: RTSCI allows objective, accurate, noninvasive and easy measurements of several parameters of skin morphology. It is useful in clinical trials, for evaluation of the effects of therapy, for preoperative evaluation of dermatological lesions, and enables visualization of subclinical and deep lesions, giving physicians the possibility of starting treatment before disease intensity increases. However, even such highly advanced ultrasound cannot completely substitute the clinical dermatological approach and the occasional need for histological diagnosis. This new method may, however, become an important adjunct method for the study of skin lesions.

Key words: dermatology surgical – dermatology ultrasound – high-resolution ultrasonography – real-time compound imaging – skin disease

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Real-time spatial compound imaging (RTSCI) was introduced in 1999. Spatial compounding is a method to reduce artefacts by taking several overlapping scans of an object from different angles, and then combining the scans to form a compound image (Fig. 1). This principle has been known since the earliest days of medical ultrasound, but is now made possible by computed beam-steering technology. RTSCI technology is used in a variety of medical applications including breast, vascular, muscular, skeletal, obstetrics/gynaecology and abdominal examinations, but the methodology has not previously been applied to the study of the skin.

Alexander and Miller were the first to introduce ultrasound (A-scan) for examination of the skin in 1979 (1). In the following applications used in dermatology practice, the majority of the studies included measurement of cutaneous thickness in a variety of normal and pathologic conditions (2). These early applications utilized transducers with ultrasonic frequencies ranging from 1.5 to 7.5 MHz. One of the first reports is from 1979 by Rukavina and Mohar (3). They used a 2MHz B-mode to image a variety of skin processes.

In the mid-1980s, higher frequency (15–20 MHz) transducers were incorporated in ultrasonic systems without real-time compound imaging to achieve higher resolution for skin examinations. It opened a new field in the examination and diagnosis of skin diseases mainly to estimate tumour thickness preoperatively in malignant melanoma (4). General experience has confirmed that 20 MHz provides a good compromise between resolution and viewing depth, while devices of 50 MHz or higher frequencies may only be suitable for scanning of the epidermis (5).

The use of high-frequency transducers in high-resolution and real-time ultrasound machines that can reach 12 or 15 MHz is a great advantage for studying superficial structures without losing resolution and penetration. These transducers
have a superficial focus. They are variable in frequency and also permit us to change the depth within a range, in cases where we need to define tumour extension in more profound layers such as muscle. This feature is not possible with other ultrasound equipment.

Within the last 5 years, the technology of skin imaging methods has developed very fast. Today, there are many commercially available options to look below the skin, e.g. optical coherence tomography (OCT) and confocal microscopy in either reflectance (RCM) or fluorescence mode. Our purpose was to examine the relevance of RTSCI in dermatology as one of these potentially new techniques. We performed an exploratory study using the RTSCI scanner on patients with various skin diseases. No data about real-time compound imaging and dermatological disease have been published previously.

Materials and Methods

Patients
We have studied the skin lesions of 21 patients with various skin diseases and 13 persons with normal skin. The mean age of the patients was 43.4 years (range 10 months–97 years), and there were 20 female (59%) and 14 male (41%). The different skin diseases were psoriasis (n = 4), venous ulcers (n = 2), haemangioma (n = 2), bullous pemphigoid (BP) (n = 2), calcinosis (n = 1), elephantiasis (n = 1), cutaneous sarcoidosis (n = 1), localized scleroderma (n = 1), mycosis fungoides (n = 1), systemic lupus erythematosus (SLE) (n = 1), muscular haematoma (n = 1), hidradenitis suppurativa (n = 1), lipoma (n = 1), polyp (n = 1) and nevus (n = 1). All skin lesions were verified afterwards by results from patient’s case records, e.g. biopsies and microbe cultures. Healthy persons provided data about nail and skin thickness for seven different anatomical regions: ventral and dorsal forearm, forehead, back (over right scapula), buttocks, medial malleolus and right index finger nail.

Participants were recruited from the Dermatology Department, Bispebjerg Hospital, Denmark in September 2001.

No restriction with regard to age, sex, duration of disease or treatment regimen was defined. Both inpatients and outpatients were examined. Persons with normal skin were recruited among medical students and hospital staff. All the persons had signed informed consent forms before entering the study. The Declaration of Helsinki principle had been followed.

Methods

Skin and nails were visualized by RTSCI (an ATL 5000 SonoCT/ATL Philips Ultrasound, WA, USA) (Fig. 2a,b). The SonoCT imaging uses computed beam-steering technology and the ultrasound beams are manoeuvred ‘off axis’ to achieve up to nine transmit angles in the course of a single scan (target mode) and compounds them in real time. In this way, several overlapping scans of an object are acquired from different view angles, and are then combined to form a compound image. Consequently, this method reduces the frame-rate, but increases the resolution.

Scanning from different angles produces different uncorrelated artefact patterns. With a special patented ‘pattern recognition technology’, it is possible to average these different patterns and suppress the acoustic artefacts to improve the image quality (Fig. 3).
The ATL 5000 SonoCT is available with various scanheads: broadband linear array, broadband curved array and broadband phased array. All have steerable and pulsed Doppler, colour Doppler (CD) and colour power angio (PA) imaging systems. Broadband scanheads are designed to send and receive signals in a wide frequency area. The beam former in the scanheads is able to control the signals; so tissue close to the transducer is scanned by relatively higher frequencies than deeper tissue.

We used a compact linear (CL) 15–7 MHz and a linear 12–5 MHz (L12-5) 50 mm broadband linear array scanhead with steerable and pulsed CD and colour PA imaging (Fig. 4), which allow visualization and quantification of a wide range of flow conditions, including slow flow states.

The L12-5 scanhead consists of 256 Piezo crystal elements arranged in lines, which give a high density of ultrasound beams. The maximum display depth is 7.9 cm and tissue penetration is 4.8 cm. The resolution at 20 dB is: axial – 0.7 mm at 20 mm and lateral – 1.0 mm at 20 mm. The CL 15–7 MHz has 128 elements and a tissue penetration of 3 cm. The axial resolution is 0.7 mm and the lateral resolution is 0.8 mm at 3 cm. Both transducers were handheld.

An assessment of nail, skin and lesions thickness was carried out by marking the borders with a cursor and measuring the distance between the marks.
An ultrasonic gel (Greenscan, Nycomed, Denmark) was applied to the aperture at the end of the probe. The ultrasound probe was gently placed over the examined area with the transducer directed perpendicular to the surface. Ultrasound images were stored on a hard disc before analysis. All ultrasound calculations were based on the mean of two measurements.

A specialist in radiology (XW), who had experience with the ATL 5000 SonoCT, performed all the examinations. A dermatology resident evaluated the skin (EAH).

Results

Skin psoriasis

The ATL 5000 SonoCT imaging obtained a good visualization of the extension of the plaques, which contain a wavy surface due to scales, a hyperechogenic superficial skin and a hypoechogenic deeper skin.

Compared with normal skin, the average skin thickness (epidermis and dermis) of each psoriasis plaque was increased. The changes were apparently mainly due to a dense layer of scales, a subepidermal low-echogenic band and diffuse enlargement of dermis itself (Fig. 5).

Nail psoriasis

We observed the appearance of hyperechoic plaques at the ventral plate in the psoriatic nails. These plaques appeared to respect the dorsal plate structure and occurred exclusively in the deeper structures. In the more affected nails, the appearance of a wavy dorsal plate with loss of definition of the ventral plate was seen (Fig. 6a, b).

We found no significant differences between normal and psoriasis nail thicknesses, but assessments with the RTSCI showed that for normal nails the mean distance between the ventral nail plate and the bone was 1.5 mm (CI 1.33–1.79). This nail–bone distance was enlarged in the nails with psoriasis involvement where the mean distance was 3.0 mm (CI 2.04–4.01) (this difference was considered to be significant at $P = 0.02$).

In psoriasis patients with no apparent nail involvement, the average distance between the ventral plate and the bone was not different from that of the normal controls.

Venous ulceration

The imaging allowed visualization of the oedema present in the dermis and subcutaneous tissue and definition of the borders of the ulcer itself.

Fig. 5. Female, 42 years; psoriasis plaque (wavy hyperechogenic epidermis and enlarged dermis, left), comparison with normal skin (NS).

Fig. 6. (a) Male, psoriatic nail; thin arrow = nail plate, thick arrow = bone. (b) Female, normal nail; thin arrow = nail plate, thick arrow = bone.
The CD and PA imaging showed an increased blood flow in the perilesional areas. In one case, the imaging with the ATL SonoCT was capable of detecting focal intradermal fluid collections beneath the ulcer, which could not be found by normal clinical examination by a physician (Fig. 7).

**Haemangioma**

We could define the diameters, the borders and the presence of macroscopic vessels inside the tumour. SonoCT imaging depicted the relationship with the surrounding structures and the superficial fascia clearly. With CD and PA imaging, we could determine if the flow was arterial or venous and the diameter of the vessels inside the tumour. In the capillary haemangioma, the blood vessels are very tiny and the flow is too slow for Doppler detection. In the case of the cavernous haemangioma, the Doppler and PA were capable of detecting the location of the blood vessels (Fig. 8a, b).

**Bullous pemphigoid (BP)**

BP is a rare, subepidermal blistering autoimmune disease where IgG autoantibodies are deposited in the basement membrane zone. The autoantibodies cause inflammation, which causes destruction of the basement membrane resulting in dermal–epidermal separation. The final result is the formation of characteristic subepidermal bullae.

In areas of pathological skin, we could clearly define the subepidermal blisters (Fig. 9). In other areas of clinically normal skin, we visualized several small areas where the epidermis was separated from the dermis by a subepidermal low-echogenic band (SELB). It is speculated that these findings could represent subclinical blisters.

Skin ulceration is a common finding among patients with BP, as a result of ruptured blisters. With the advanced ultrasound equipment, it was possible to define the diameters and depth of the ulcer and to detect if there was any oedema in the dermis or in the subcutaneous tissue.

Fig. 7. Female, 53 years; erysipelas lesion in the anterior leg with a subcutaneous collection. The fluid collection is seen as anechogenic or hypoechogenic area with irregular borders between the arrows.

Fig. 8. (a) Male, 2 years; cavernous haemangioma in the scalp. A hypoechogenic tumour with anechogenic vascular structures inside. (b) Male, 2 years; cavernous haemangioma colour Doppler in the scalp, same patient (a) with notorious vessels.
Haematoma
One patient had a tumour located on the upper part of his thigh. With the RTSCI, it was possible to see that the tumour was located in the subcutaneous tissue and had a homogeneous anechogetic signal. A trauma was seen in the skin over the anechogetic fluid collection (Fig. 10).

Hidradenitis suppurativa
The RTSCI was carried out in an area with puckered and scarring skin as a result of chronic inflammation. The image showed a heterogeneous tissue with high-echogenic lines with dark areas in between. These lines probably represent fibrosis and the low-echogenic areas represent sinuses or abscesses (Fig. 11).

Lipoma
The lipoma was seen as a very homogeneous solid structure within the subcutaneous tissue with a hyperechogenic signal (Fig. 12).

Fibroepithelial polyps
This polyp is shown with the three-dimensional SonoCT ultrasound imaging system. Several 2D images are compounded to 3D data sets, which contain more information about the polyps’ volume and surface than normal 2D imaging (Fig. 13).

Lymphoedema–elephantiasis
Lymphoedema is often accompanied by some epidermal hyperproliferation and subcutaneous...
fibrosis, which can be seen as an increase in echogenicity. This was visualized in our case of very severe oedema, which compromised all the layers of the dermis in a uniform distribution. With PA and CD, we found an increase in blood flow in the entire dermis.

**Calcinosis**
This is a disease with subcutaneous calcium deposits, seen as nodules. In response to this foreign material, the skin surrounding the calcium becomes painful, red and sometimes chronically inflamed. The localization of the calcium deposits was defined clearly by RTSCI with an L12-5 MHz transducer. Because of the acoustic shadowing due to the solid calcium nodules, no structure was seen in the layers beneath the calcium deposits.

**Nevus**
Nevus could clearly be separated from the surrounding skin and it was easy to define the diameters and the visible borders of the structure. With CD and PA, it was possible to see the extension and presence of vessels inside the tumour.

**Diseases with no specific findings**
One patient had mycosis fungoides in an eczematous form with nonspecific, flat, red, itchy eczematous areas. When examining the skin with ultrasound, no special characteristic features were found except for diffuse changes of the echogenicity in the affected area. The two patients with autoimmune disease (localized scleroderma and SLE) and the patient with cutaneous sarcoidosis did not show any significant structural changes except inflammation.

**Discussion**
Ultrasound may be of use in dermatology, by giving the physicians a possibility to visualize structures in the skin. Thus, it could ideally be a noninvasive alternative to skin biopsy. Skin biopsy provides a detailed description of histological data, but may have the disadvantage of possible pain, infection, scarring and a limited field of view. Biopsies are naturally less suitable for longitudinal studies of how lesions evolve. At present, ultrasound cannot, however, in itself substitute the clinical dermatological approach combined with histology, but this study suggests that important auxiliary data can be provided by RTSCI.

In several cases, the high resolution ultrasound gave relevant additional information about structures that were not suspected by the attending physicians. The knowledge of these subclinical findings is useful for diagnosis and planning of treatment strategies. In addition, it may be useful in the assessment of disease status and severity. In erysipelas, the RTSCI may be able to detect intradermal fluid collections, which are not suspected clinically. The ultrasound imaging allows the identification of diameters and the depth of ulcers and fluid accumulation, which makes puncture or drainage of intradermal fluid possible. The presence of an intradermal abscess can explain the failure of treatment in some cases.

In BP structures compatible with subclinical, blisters were found and these structures may represent an early stage of the disease. If verified, these observations suggest an important role of RTSCI in the management of blistering diseases, opening the possibility of treatment before visible blisters develop and potentially shortening both the duration and severity of the disease.

Measurement of skin thickness was possible with the RTSCI and showed significant difference between psoriasis and normal skin. This finding is in accordance with the previous ultrasonography observations (6, 7).

The differences of the nail–bone distances between psoriasis and normal nails have not previously been published, but await independent
confirmation in further nail studies. The lesions of psoriasis plaque have various degrees of hyperkeratosis and scaling. A very thick layer of scales and a severe hyperkeratosis can disturb the ultrasound by giving a strong entrance echo, which renders further examination impossible. This was not a problem with the RTSCI broadband scanhead due to its variability in frequency inside the same probe.

It may be speculated that this new generation of ultrasound equipment will be a relevant tool to assess the effect of, e.g. psoriasis treatment, by making objective measures of decreased scaling and hyperkeratosis available.

In diseases with atrophy or hypertrophy such as localized scleroderma, SLE and cutaneous sarcoidosis, measurements of thickness and echogenicity with RTSCI may also be a supplement to clinical evaluation of treatment effects.

In addition, the method offers further possibilities of studying skin tumours in vivo. In haemangioma and nevus, RTSCI gives information about tumour thickness and structure, and identifies intradermal extension, which is potentially useful for the planning of surgical procedures and for monitoring. A previous study of skin tumours found that the sonographic pattern corresponded to the surgical findings and the histopathologic picture (8). Harland et al. investigated 29 basal cell papillomas and 25 melanomas with high-resolution ultrasound (20 MHz B-scan imaging). They concluded that it was possible to differentiate melanoma from basal cell papillomas, but not from benign naevi by ultrasound (9). It may be speculated that the enhanced image quality of RTSC will allow further refinement of diagnosis.

For the more generalized skin diseases such as SLE, sarcoidosis and mycosis fungoides, the RTSCI gives little information about specific skin structures; however, in combination with clinical examination it may be useful when deciding a biopsy area.

Conclusion

This study has presented a descriptive review of potential new areas for ultrasound examination of the skin and subcutaneous tissue enabled by technological development. It is suggested that RTSCI allows objective, accurate, noninvasive and easy measurements of skin thickness and morphology, which may become useful in clinical trials and for the evaluation of the effects of therapy.

The main advantage of RTSCI compared with conventional high-frequency ultrasound Dermascan, OCT and confocal microscope is the tissue penetration depth of 48 mm. This may be compared with 0.9–1.0 mm for the OCT and RCM and 10–30 mm for the conventional high-frequency ultrasound Dermascan. This makes examinations of dermis, subcutaneous tissue, tendons and muscle possible, but does not provide imaging of the detailed structures of the epidermis and nails. The disadvantage of the machine is the cost, which is nearly five times that of the Dermascan and four times that of the confocal microscope and OCT. The visualization of the various skin pathologies with the new generation of ultrasound machines and probes may encourage more physicians to use it as a tool in their daily practice, and maybe more ultrasonographers may develop an interest in the visualization of various skin structures.

The clinical correlation is an important feature in any such venture, and may offer advantages for the operator’s interpretation of the examination much in the same way as in any other imaging modality, e.g. simple X-rays.

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