Development and Evaluation of a High-Frequency Ultrasound-Based System for In Vivo Strain Imaging of the Skin

Michael Vogt, Member, IEEE, and Helmut Ermert, Fellow, IEEE

Abstract—The elastic properties of skin are of great interest in dermatology because they are affected by many pathological conditions. In this paper, a technique for in vivo mechanical strain imaging of the skin based on high-frequency ultrasound (HFUS) is presented. Elastic skin properties are assessed applying suction to the skin surface with a stepwise increased vacuum and estimating the resulting displacements in a spatially resolved manner. Acquired radio frequency (RF) echo signals and their envelope are analyzed for this purpose. A computer-controlled vacuum system with a digital pressure control loop was developed for precise and reproducible deformation. In a first processing step, the skin surface is segmented. Local axial strains inside the skin are estimated from axial displacements, which are estimated from consecutive echo signal frames analyzing the phase of the complex cross correlation function of analytical echo signals. Furthermore, speckle tracking is applied to estimate axial and lateral displacements and to quantify axial and lateral strains. The correlation coefficient of windowed echo signals compensated for displacements are used as a measure to validate the estimated strains, which is essential to accomplish reliable in vivo measurements. Phantom experiments were performed to validate the proposed technique. Results of in vivo measurements are presented, showing the potential for mechanical strain imaging in the skin in vivo.

I. INTRODUCTION

Skin diseases such as psoriasis and scleroderma—as well as skin burnings, skin aging, and changes of the epidermal hydration—cause changes in skin elasticity [1]–[5]. For this reason, tactile investigations are routinely performed during dermatological examinations, but the results strongly depend on the individual sense and experience of the physician. Presently, available tools for the measurement of elastic skin properties are based on applying external mechanical deformations (traction, torsion, suction, etc.) and analyzing the resulting displacement of only the skin surface using optical measurements techniques [1]–[3], [6]. Lack of depth information as well as the limited spatial resolution, the latter being a result of limited measurements each performed at a single point at the skin surface, are the major drawbacks of the currently available techniques. High-frequency ultrasound (HFUS), however, is a valuable tool to image the morphology of small organs such as skin and eye in depth noninvasively with high resolution [7]–[19].

Different attempts already have been made to assess elastic properties of the skin applying HFUS. Diridollou et al. [4] used 20 MHz ultrasound for skin imaging accompanied by the application of suction to the skin surface. The skin surface, the border between the dermis and the subcutaneous fat, and the border between the subcutaneous fat and the muscle were detected and changes in skin layers thickness were quantified and analyzed. Furthermore, the results of measurements along a single line were fitted to an analytical, elastic membrane model to determine intrinsic mechanical parameters of the skin [5]. A similar measurement technique was applied by Hendriks et al. [20], measuring the deformation of the dermis based on ultrasound images. Results of these analyses were fitted to a finite-element model. Pan et al. [21], [22] acquired echo signals with a 40 MHz ultrasound biomicroscope while stretching the skin surface transversely. Applied stress and intensity changes in ultrasound images were analyzed. Furthermore, ultrasound attenuation and backscattering coefficients were measured and correlated with elastic skin properties.

Apart from these approaches, ultrasound elastography, first introduced in 1991 by Ophir et al. [23], allows one to image elastic properties of tissues over depth. An external deformation of the tissue is induced, and the resulting displacements are measured using ultrasound. From the displacement estimates, the mechanical strain inside the tissue is derived. As a result, higher strain magnitudes are found in regions of softer tissue and lower strain magnitudes in regions of harder tissue. The problem in applying this concept to the assessment of elastic skin properties is to induce a mechanical excitation in an appropriate way under in vivo conditions. Cohn et al. [24]–[26] implemented an ultrasound elasticity microscope using 50 MHz ultrasound to assess elastic properties of tissue specimens for applications in dermatology, ophthalmology, pathology and tissue engineering. Axial and lateral strains, estimated through speckle tracking, were used for elasticity reconstructions.

Zheng and Mak [27] implemented an ultrasound indentation system for the measurement of tissue deformation and
over depth along a single line, acquiring RF echo signals using ultrasound with frequencies up to 10 MHz. They fitted measured deformations to a mechanical model. Furthermore, they implemented a 50 MHz ultrasound compression system for studying the biomechanical properties of articular cartilage, based on the analysis of deformations [28], [29].

In dermatology, HFUS in the 20 MHz range and above is already being advantageously applied for noninvasive and high-resolution imaging of skin morphology and allows preoperative measurements of the tumor thickness as well as the progression and treatment of many skin diseases [7], [9], [10], [14]–[17]. Capability to furnish spatially resolved information on the elastic behavior of the tissue, additional to the morphological one, that may enhance the noninvasive evaluation of the skin in vivo, is among the major desirable characteristics of a HFUS imaging system. In this paper, the development and evaluation of a high-frequency ultrasound system for spatially resolved mechanical strain imaging in the skin in vivo is presented. Using HFUS in the 20 MHz range, RF echo signals are acquired during a step-wise decreased pressure at the skin surface. Local strains in the skin and the subcutaneous fat are calculated over depth and over the lateral coordinate, analyzing consecutive echo signal frames. High resolution axial and lateral strain images are obtained, which give information about mechanical skin properties at a microscopic level.

II. Materials and Methods

In this section, the developed HFUS imaging system and the implemented approaches for mechanical strain assessment are presented.

A. High-Frequency Ultrasound Strain-Imaging System

We have developed a strain imaging system, which is based on a commercial 20 MHz ultrasound scanner for skin imaging applications (DUB 20, taberna pro medicum GmbH, Lüneburg, Germany) [30], [31]. Using ultrasound and applying phase sensitive measurement concepts, axial displacements in the direction of sound propagation generally can be measured much more sensitive than displacements in the perpendicular directions. For this reason, it is intended to induce mainly axial deformations during the measurements. This is achieved by sucking the skin through a relatively large slot into a vacuum chamber, which is placed at the skin surface, and performing pulse-echo measurements over depth. While the pressure inside the chamber is decreased stepwise, the skin is increasingly drawn into the slot and imaged after each pressure change with a mechanically scanned HFUS transducer inside the chamber (Fig. 1). In order to bring about well-defined boundary conditions, the system was equipped with a vacuum pump system with a digital pressure control loop for reproducible measurements. For all strain measurements, a step-wise, increased vacuum with the nominal pressure scheme shown in Fig. 2 was applied. The applicator was placed at the top of the skin area under investigation. During intervals of 10 s duration, the pressure was decreased by 12.5 mbar after each lateral scan. The measured pressure in Fig. 2 shows that the nominal pressure is properly reached within these intervals.

Mechanical scans are performed inside the chamber along the lateral coordinate $x$ with a fixed-focus, single-element transducer. This transducer, which is driven by a pulser/receiver, has a 21 MHz center frequency, 72% relative bandwidth ($−6 \text{ dB}$), 6.3 mm aperture diameter, 15.2 mm focus distance, and 2.64 mm depth of field ($−6 \text{ dB}$).

The applicator of the ultrasound scanner fulfills the function of the above mentioned vacuum chamber, whereby the skin is sucked into a slot at the bottom of the applicator. In order to achieve predominantly axial displacements in the region of interest (ROI), a slot with a dimension of 20 mm $\times$ 6 mm (lateral/elevational direction) was chosen, which is large compared to the lateral scan path length and the elevational resolution of the ultrasound system. However, with significantly smaller slots relatively large lateral and elevational displacements would appear [4], [5], [20]. Ultrasound waves are coupled to the skin through a water bath, which is located beneath the air column inside the chamber (Fig. 1); 384 A-lines are acquired along a lateral dimension of 12.5 mm, resulting in a lateral spacing $\Delta x = 33 \mu\text{m}$ between adjacent A-lines. At each position, RF echo signals are digitized using an analog to digital converter (100 MHz sampling rate, 8 bits amplitude resolution) and fed into the same com-
computer, which controls the data acquisition and assigns the predefined nominal pressure curves. Each A-line consists of 1024 samples, covering a depth range of 8.2 mm, which allows imaging the skin as well as the underlying fat and the top of the muscle [Fig. 3(a)]. High-resolution imaging is performed with a minimum axial (−6 dB) resolution \( \delta_x = 44 \ \mu \text{m} \) and a minimum lateral (−6 dB) resolution \( \delta_y = 139 \ \mu \text{m} \) at the transducer focus, which was quantified from measurements at a string phantom (tungsten wire with 7-\( \mu \text{m} \) diameter in water).

B. Echo Signals Acquisition

During the stepwise decrease of the pressure inside the chamber, frames of RF echo signals \( s_{p_v}(t, x) \) are acquired at lateral positions \( x \) and over time of flight \( t \), while a constant pressure \( p_v \) is applied. The complex analytical echo signals \( s_{p_v}(t, x) \) are obtained applying the Hilbert transform \( H\{\ldots\} \):

\[
\begin{align*}
  s_{p_v}(t, x) &= s_{p_v}(t, x) + i \cdot H\{s_{p_v}(t, x)\}, \\
  H\{s_{p_v}(t, x)\} &= \frac{1}{\pi} \int_{-\infty}^{\infty} \frac{s_{p_v}(t', x)}{t - t'} dt'. 
\end{align*}
\]

(1)

B-mode images \( b_{p_v}(z, x) \) (i.e., the envelope of the RF echo signals) are calculated as the magnitude of the analytical echo signals \( s_{p_v}(t, x) \) at each lateral scan position \( x \), scaling the time of flight \( t \) by the speed of sound \( c \) [30], [31], see Fig. 3(a):

\[
b_{p_v}(z, x) = \left| s_{p_v}(t, x) \right|_{t=2/cz}.
\]

(2)

C. Mechanical Strain Assessment

As already mentioned above, displacement estimates are the basis for the assessment of mechanical strains inside the tissue. A phase-sensitive correlation method for the estimation of the axial displacement based on the analysis of the acquired RF echo signals is presented below. Furthermore, an efficient two-dimensional (2-D) speckle tracking approach based on the analysis of spectral information of the envelope of the acquired echo signal frames (i.e., the B-mode images) is introduced.

At the center of the slot, the displacements of the skin surface are expected to be predominantly in axial direction \( z \), i.e., perpendicularly to the skin surface and along the direction of sound propagation. Because the tissue is considered to be almost incompressible and the muscle tissue is found to remain mainly in its initial position during the applied suction, in general displacements \( \Delta x_{\text{displ}} \) and \( \Delta y_{\text{displ}} \) in lateral and elevational directions \( x \) and \( y \), respectively, appear in addition to the displacements \( \Delta z_{\text{displ}} \) in axial direction \( z \). The displacements of the skin and the subcutaneous fat relative to the transducer are significantly large, whereas the underlying muscle tissue can be assumed to remain effectively in its initial position. A key limitation of displacement estimation techniques using phase-sensitive, time-delay estimation to analyze ultrasound echo signals is their failure to estimate large displacements. Therefore, the skin surface is segmented in each acquired frame, and the echo signals at different pressure levels are aligned relative to the segmented skin surface, see Fig. 3(b). To avoid artificially introduced shear strains between neighboring echo signal lines, a low-pass filter is applied to the segmented contour data points before echo signal alignment.

In a first approach, a phase-sensitive method is applied to estimate the axial displacements \( \Delta z_{\text{displ}} \) inside the
skin and inside the subcutaneous fat, tracking RF echo signals in adjacent windows over depth $z$, starting from the skin surface. In a second approach, axial and lateral displacements $\Delta z_{\text{displ}}$ and $\Delta x_{\text{displ}}$, respectively, are estimated. Speckle, which is inherent in the B-mode image frames, is tracked in adjacent windows over depth $z$ and over the lateral coordinate $x$, starting from the skin surface at the center of the slot, see Fig. 3(b).

In both approaches the estimated displacements are accumulated along the analyzed adjacent windows. Axial and lateral strains are calculated as spatial derivatives of the accumulated axial and lateral displacements. The mechanical strain, which is estimated in each window, is assigned to the pixels of a parametric strain image. Because the deformation of the skin can be complex in general, positive strains (elongations) as well as negative strains (compressions) can occur.

D. Skin Surface Segmentation and Echo Signal Alignment

In a first processing step, the skin surface is independently segmented in each B-mode frame $b_{pv}(z, x)$ at constant pressure $p_v$. A threshold-based segmentation is applied because of the high contrast between the water path and the skin surface in the B-mode images. In the implemented approach, constraints concerning the smoothness of the skin surface are considered in order to reject cross sections of hairs, which are sometimes visible above the skin surface, see Fig. 3(a). Furthermore, as already mentioned, a low-pass filter is applied to the segmented contour to inhibit artificially introduced shear stresses. As a result, surface contours $c_{pv}(x)$ are obtained, which already deliver information about the overall skin surface elevation, see Fig. 3(a). In a second processing step, the analytical echo signals $s_{pv}(t, x)$ are aligned relative to the segmented skin surface contours, and the B-mode images $b_{pv}(z, x)$ are recalculated, see Fig. 3(b). Displacements inside the skin relative to the skin surface rather than absolute displacements relative to the transducer are analyzed with the strain estimation approaches introduced below. The skin surface is used as the starting point for the displacement estimations.

E. Phase-Sensitive Axial Strain Estimation

Ultrasound can advantageously be applied for sensitive time delay measurements, and thus for displacement estimations in the axial direction (i.e., in direction of sound propagation $z$), performing a phase-sensitive analysis of the echo signal frames.

In a first approach, lateral displacements are neglected (i.e., $\Delta x_{\text{displ}} = 0$ is assumed), and only axial displacements $\Delta z_{\text{displ}}$ are estimated over depth $z$. This is done by analyzing the analytical echo signals $s_{pv}(t, x)$ and $s_{pv+1}(t, x)$, which result from acquisitions under pressures $p_1 = p_v$ and $p_2 = p_{v+1}$, in axial windows. Axial displacements are tracked and accumulated over depth, starting with the analysis of echo signals directly below the skin surface.

Afterward, axial displacements between the first analytical echo-signal frame $s_{pv}(t, x)$ and the second analytical echo-signal frame $s_{pv+1}(t, x)$ are estimated in axially adjacent windows with the axial window size $\Delta z_{\text{size}}$. For each displacement calculation, $s_{pv}(t, x)$ is analyzed in a $\Delta z_{\text{shift}}$-shifted window, relative to the previous window, and $s_{pv+1}(t, x)$ in a $\Delta z_{\text{shift}} + \Delta z_{\text{displ}}$-shifted window, with the estimated displacement $\Delta z_{\text{displ}}$ in the previous window, see Fig. 3(b). Accumulated axial displacements $\Delta z_{\text{displ}}$ are calculated in each window as the sum over all axial displacements in the previous windows. In each pair of windows, the displacement is estimated analyzing the complex cross-correlation function $c_{s_{pv+1}, s_{pv}}(t, x)$ of the two analytical echo signals $s_{pv}(t, x)$ and $s_{pv+1}(t, x)$ with respect to the time of flight $t$, see Fig. 4 (a) and (b):

$$c_{s_{pv+1}, s_{pv}}(t, x) = \int_{t'} s_{pv}(t', x) \cdot s_{pv+1}^*(t + t', x)dt'$$

(3)

Presuming the correlation between both windowed analytical echo signals is high, for which small local strains are required, the two signals can be considered to be time-shifted versions of each other (i.e., $s_{pv+1}(t, x) = s_{pv}(t - \Delta t, x)$), with the time of flight shift $\Delta t = 2/c \cdot z_{\text{displ}}$. Under these conditions, the phase of the complex cross-correlation function $c_{s_{pv+1}, s_{pv}}(t, x)$ depends on $\Delta t$ [24], [32], [33]:

$$c_{s_{pv+1}, s_{pv}}(t, x) = e^{-i\omega_0(t - \Delta t)} \cdot \int_{t'} s_0(t', x) \cdot s_0^*(t + t' - \Delta t, x)dt'$$

(4)
In (4), \( s_0(t, x) \) is the baseband signal of the analytical echo signal \( s_{t+p}^e(t', x) = s_0(t, x) \cdot e^{-i\omega_0 t} \) with the carrier-signal frequency \( \omega_0 \). A time-shift estimate \( \Delta t \) is efficiently and accurately calculated using an iterative search for the root of the phase of \( c_{t+p+1}^e(t, x) \), a method proposed by Pesavento et al. (phase root seeking algorithm) [33]–[35]. In this approach, the complex cross-correlation function \( c_{t+p+1}^e(t, x) \) is calculated at time lag zero, i.e., for \( t = 0 \), first. Under the knowledge that the slope of the phase arg \( \{c_{t+p+1}^e(t, x)\} \) is equal to the carrier signal frequency \( \omega_0 \), see (4), time-shift estimates \( \Delta t \) and, thus, axial displacement estimates \( \Delta z_{\text{displ}} = c/2 \cdot \Delta t \) can be calculated applying a Newton iteration.

The spatial derivative of the accumulated axial displacement estimates \( \Delta z'_{\text{displ}} \) relative to the axial coordinate \( z \) delivers estimates \( \dot{e}_z \) of axial strains, see Fig. 4(c):

\[
\dot{e}_z = \frac{\partial \Delta z'_{\text{displ}}}{\partial z}. 
\]

(5)

In the implementation, axial strains are estimated determining the slopes of linear regression fits of the accumulated estimated axial displacements \( \Delta z'_{\text{displ}} \) over depth \( z \).

In order to obtain an unambiguous phase information in (3), the time shift \( \Delta t \) must be limited. If positive and negative strains (i.e., elongations as well as compressions) occur, the following conditions must be fulfilled considering the wavelength \( \lambda_0 = 2\pi \cdot c/\omega_0 \) at the carrier signal frequency \( \omega_0 \), see (4) and (5):

\[
|\Delta t| \leq \frac{\pi}{\omega_0} \Rightarrow |\Delta z_{\text{displ}}| = \frac{c}{2} \cdot |\Delta t| \leq \frac{\lambda_0}{4} \Rightarrow |\varepsilon_z| \approx \frac{|\Delta z_{\text{displ}}|}{\Delta z_{\text{shift}}} \leq \frac{\lambda_0}{4 \cdot \Delta z_{\text{shift}}}. 
\]

(6)

For all phase-sensitive, axial-strain estimations in this paper, an axial window size \( \Delta z_{\text{size}} = 80 \, \mu m \) and an axial window shift \( \Delta z_{\text{shift}} = 80 \, \mu m \) were chosen. Under these conditions, considering the center frequency \( f_0 = 21 \, \text{MHz} \) of the system, the requirements concerning an unambiguous phase information, which are given by (6), are satisfied for axial strains \( \varepsilon_z \leq 24\% \). However, pressure changes between the echo signal acquisitions are limited during the measurements to obtain much smaller axial strains in the range up to a few percent only to avoid decorrelation. Axial strains were estimated as the slopes of linear regression fits over displacement estimates in 10 axially adjacent windows. The resulting strain images were averaged over a kernel with an axial and lateral dimension of 800 \( \mu m \) and 330 \( \mu m \), respectively.

F. 2-D Speckle Tracking-Based Axial and Lateral Strain Estimation

As shown above, the axial displacements can be measured by estimating time of flight shifts using phasesensitive techniques. However, the applicability of such approaches is subject to the condition that lateral and elevational displacements perpendicular to the direction of sound propagation should be negligibly small.

Lateral displacements result in lateral shifts of echo signal between adjacent A-lines. In a second approach, lateral displacements \( \Delta x_{\text{displ}} \) and axial displacements \( \Delta z_{\text{displ}} \) are estimated. This is done by tracking speckle [31], [36]–[38] in the B-mode images \( b_{p_v}(z, x) \) and \( b_{p_v+1}(z, x) \), which result from acquisitions under pressures \( p_1 = p_v \) and \( p_2 = p_{v+1} \), respectively. Axial and lateral displacements are tracked and accumulated over depth \( z \) and over the lateral scan position \( x \), starting with the analysis of B-mode frames directly below the skin surface at the center of the slot. Afterward, the axial and lateral displacements between the first B-mode frame \( b_{p_v}(z, x) \) and the second B-mode frame \( b_{p_{v+1}}(z, x) \) are estimated in axially and laterally adjacent windows with the axial and lateral window sizes \( \Delta z_{\text{size}} \) and \( \Delta x_{\text{size}} \). For each displacement calculation, \( b_{p_v}(z, x) \) is analyzed in a \( \Delta z_{\text{shift}} \) axially shifted window, relative to the previous window, and \( b_{p_{v+1}}(z, x) \) in a \( \Delta z_{\text{shift}} + \Delta z_{\text{displ}} \) and \( \Delta x_{\text{shift}} + \Delta x_{\text{displ}} \) shifted window with the estimated displacements \( \Delta z_{\text{displ}} \) and \( \Delta x_{\text{displ}} \) in the previous window, see Fig. 3(b). Accumulated axial and lateral displacements \( \Delta z_{\text{displ}} \) and \( \Delta x_{\text{displ}} \) are calculated in each window as the sum over all axial and lateral displacements in the previous windows. In each pair of windows, displacements are estimated analyzing the phase difference between the two spectra \( B_{p_v}(\omega_z, \omega_x) \) and \( B_{p_{v+1}}(\omega_z, \omega_x) \) of the two B-mode images \( b_{p_v}(z, x) \) and \( b_{p_{v+1}}(z, x) \), see Figs. 5(a) and (b) [31]:

\[
B_{p_v}(\omega_z, \omega_x) = \int \int b_{p_v}(z, x) \cdot e^{-i(\omega_z z + \omega_x x)} \, dz \, dx, \\
\mu = v, v + 1.
\]

(7)

As long as the correlation between both B-mode images is high, for which small local strains are again required, they can be considered to be spatially shifted versions of each other, i.e., \( b_{p_{v+1}}(z, x) = b_{p_v}(z - \Delta z_{\text{displ}}, x - \Delta x_{\text{displ}}) \). Thus, the phase difference \( \Delta \phi(\omega_z, \omega_x) \) between the two
spectra is a linear function of the spatial frequencies \( \omega_z \) and \( \omega_x \), see Fig. 5(c) [31], [36], [39]:

\[
\Delta \varphi(\omega_z, \omega_x) = \arg \left\{ B_{x,z}(\omega_z, \omega_x) \right\} - \arg \left\{ B_{x,z+1}(\omega_z, \omega_x) \right\} = \omega_z \cdot \Delta \hat{z}_{\text{disp}} + \omega_x \cdot \Delta \hat{x}_{\text{disp}}.
\]

Taking only the phase differences \( \Delta \varphi_n \) at those spatial frequencies \( \omega_z,n \) and \( \omega_x,n \) into account, where the spectra show sufficiently high spectral energy for reliable phase measurements, displacement estimates \( \Delta \hat{z}_{\text{disp}} \) and \( \Delta \hat{x}_{\text{disp}} \) are obtained by linear regression fits:

\[
\sum_n \left( \Delta \varphi_n - (\omega_z,n \cdot \Delta \hat{z}_{\text{disp}} + \omega_x,n \cdot \Delta \hat{x}_{\text{disp}}) \right)^2 \overset{!}{=} \min,
\]

\[
\begin{pmatrix}
\Delta \hat{z}_{\text{disp}} \\
\Delta \hat{x}_{\text{disp}}
\end{pmatrix} = \begin{pmatrix}
\sum_n \omega_z,n^2 & \sum_n \omega_z,n \cdot \omega_x,n \\
\sum_n \omega_x,n \cdot \omega_z,n & \sum_n \omega_x,n^2
\end{pmatrix}^{-1} \begin{pmatrix}
\sum_n \omega_z,n \cdot \Delta \varphi_n \\
\sum_n \omega_x,n \cdot \Delta \varphi_n
\end{pmatrix}.
\]

The spatial derivatives of the accumulated axial and lateral displacement estimates \( \Delta \hat{z}_{\text{disp}}' \) and \( \Delta \hat{x}_{\text{disp}}' \) relative to the axial and lateral coordinates \( z \) and \( x \) deliver estimates \( \hat{\varepsilon}_z \) and \( \hat{\varepsilon}_x \) of the axial and lateral strains, compare (5):

\[
\hat{\varepsilon}_z = \frac{\partial \Delta \hat{z}_{\text{disp}}'}{\partial z}, \quad \hat{\varepsilon}_x = \frac{\partial \Delta \hat{x}_{\text{disp}}'}{\partial x}.
\]

In the implementation, axial and lateral strains are estimated determining the slopes of linear regression fits of the accumulated estimated axial and lateral displacements \( \Delta \hat{z}_{\text{disp}}' \) and \( \Delta \hat{x}_{\text{disp}}' \) over depth \( z \) and over the lateral coordinate \( x \).

The B-mode images, which are analyzed for speckle tracking, are sampled in intervals \( \Delta z \) over depth, which depends on the echo signal sampling rate, scaled by the speed of sound. The sampling interval \( \Delta x \) in lateral direction is equal to the lateral spacing between adjacent A-lines. Spectra are calculated applying the discrete Fourier transform (DFT). Thus, the maximum spatial frequencies \( \omega_z,\text{max} = \pi/\Delta z \) and \( \omega_x,\text{max} = \pi/\Delta x \), which are analyzed, depend on the sampling intervals as is shown in Fig. 5(b). For unambiguous measurements, axial displacement \( \Delta z_{\text{disp}} \) and lateral displacement \( \Delta x_{\text{disp}} \) must be limited too. If positive and negative strains (i.e., elongations as well as compressions) occur, the conditions given in (11) must be fulfilled to obtain unambiguous phase differences, see (7) and (8), compare (6).

Furthermore, the lateral spacing \( \Delta x \) between the adjacent A-lines must be matched to the lateral resolution \( \delta_x \) of the system to fulfill the requirements of the sampling theorem. An adequate sampling of the lateral sound beam characteristics is required to allow lateral displacements tracking with the approach introduced above. In the implemented system, \( \Delta x = 33 \mu m \) is much smaller than the minimum lateral (–6 dB) resolution \( \delta_x = 139 \mu m \). Under this condition, an adequate lateral sampling is performed.

For all speckle tracking analyses, axial and lateral window sizes \( \Delta z_{\text{size}} = 256 \mu m \) and \( \Delta x_{\text{size}} = 530 \mu m \) and axial and lateral window shifts \( \Delta z_{\text{shift}} = 128 \mu m \) and \( \Delta x_{\text{shift}} = 260 \mu m \) were chosen. Thus, with the axial and lateral sampling intervals \( \Delta z = 8 \mu m \) and \( \Delta x = 33 \mu m \), conditions for unambiguous phase differences given by (11) could be obtained for axial and lateral strains \( \varepsilon_z \leq 6.3\% \) and \( \varepsilon_x \leq 13\% \). However, the maximum strains, which are applied during the measurements, are smaller to avoid decorrelation, as already mentioned above. Axial and lateral strains were estimated as the slopes of linear regression fits over displacement estimates in 10 axially and laterally adjacent windows, and the resulting strain images were averaged over a kernel with an axial and lateral dimension of 256 \( \mu m \) and 520 \( \mu m \), respectively.

G. Validation of the Reliability of Strain Estimates

The above discussed displacement estimation approaches are based on the assumption that the local strains are small to ensure that the correlation of the analyzed echo signal and B-mode frames is sufficiently high. Only under these conditions, time shifts \( \Delta t \) and axial and lateral displacements \( \Delta z_{\text{disp}} \) and \( \Delta x_{\text{disp}} \) can be assumed to occur as a result of the tissue deformation.

However, it is essential to obtain reliable strain estimates to allow a differentiation of hard and soft tissues analyzing strain images. Thus, it is proposed to calculate the correlation coefficients \( \rho_{\text{echo}} \) and \( \rho_{\text{B-mode}} \), respectively, of aligned echo signals and B-mode images, i.e., after compensation for accumulated estimated time shifts and displacements \( \Delta t' \), \( \Delta z_{\text{disp}}' \), and \( \Delta x_{\text{disp}}' \), as measures for the reliability of the calculated strain estimates in each window as shown in (12) (see next page).

In order to obtain reliable strain images, we retain only the strain estimates with correlation coefficients \( \rho > 90\% \) for further analysis and reject the others. A threshold of 90% was found to be reasonable by plotting pairs of analyzed A-lines, visually analyzing the similarity between the echo signals, and taking the calculated correlation coefficients into consideration.

H. Measurements

Measurements on speckle phantoms with regions of different elasticity were performed in order to prove the implemented system. Phantoms were made of gelatin and agar with concentrations of 3 g per 100 ml. The gelatin is relatively soft compared to the agar. In both materials, silica gel particles with a mean diameter of 15 \( \mu m \) (Merck KgaA, Darmstadt, Germany) were added with a concentration of 1 g per 100 ml as scatterers to obtain homogeneous backscattering. After phantom validation, experiments on healthy skin and on skin lesions were performed to evaluate the potential of the developed technique for in vivo applications.
\[ |\Delta x_{\text{displ}}| \leq \frac{\pi}{\omega_{x,\text{max}}} \Rightarrow |\Delta z_{\text{displ}}| \leq \Delta z \Rightarrow |\varepsilon_z| \approx \frac{|\Delta z_{\text{displ}}|}{\Delta z_{\text{shift}}} \leq \frac{\Delta z}{\Delta z_{\text{shift}}}, \]
\[ |\Delta x_{\text{displ}}| \leq \frac{\pi}{\omega_{x,\text{max}}} \Rightarrow |\Delta x_{\text{displ}}| \leq \Delta x \Rightarrow |\varepsilon_x| \approx \frac{|\Delta x_{\text{displ}}|}{\Delta x_{\text{shift}}} \leq \frac{\Delta x}{\Delta x_{\text{shift}}}. \]

\[
\rho_{\text{echo}} = \frac{\text{cov} \left( s_{p_n}(t), s_{p_{n+1}} \left( t + \Delta t' \right) \right)}{\sqrt{\text{var} \left( s_{p_n}(t) \right) \cdot \text{var} \left( s_{p_{n+1}} \left( t + \Delta t' \right) \right)}},
\]
\[
\rho_{\text{B-mode}} = \frac{\text{cov} \left( b_{p_n}(z, x), b_{p_{n+1}} \left( z + \Delta z'_{\text{displ}}, x + \Delta x'_{\text{displ}} \right) \right)}{\sqrt{\text{var} \left( b_{p_n}(z, x) \right) \cdot \text{var} \left( b_{p_{n+1}} \left( z + \Delta z'_{\text{displ}}, x + \Delta x'_{\text{displ}} \right) \right)}}.
\]

Fig. 6. Gelatin/agar speckle phantom. (a) One B-mode image out of series of acquisitions during stepwise decreased pressure at the surface, contour plot \(c_{p_n}(x)\). (b) Axial strains \(\varepsilon_z\) (phase-sensitive strain estimation). (c) Axial strains (left) \(\varepsilon_z\) and lateral strains (right) \(\varepsilon_x\) (speckle tracking).

III. RESULTS

A. Phantom Experiments

In Fig. 6(a), a B-mode image, which was acquired on a speckle phantom with gelatin on the left-hand side and agar on the right-hand side, is shown. Due to the homogeneous backscattering, the two regions cannot be distinguished from each other in the single B-mode image. The contour plot in Fig. 6(a), in which the segmented surface contours are plotted at different applied pressures, already reveals that the mechanical properties at the left- and the right-hand side of the phantom are different. The elevation of the surface of the gelatin is large compared to the surface elevation of the agar. Because the bottom side of the phantom is fixed relative to the transducer, each of the two structures is homogeneous over depth, and the boundary conditions are the same for both objects, it can be concluded that the gelatin is much softer than the agar. The goal of the implemented system is to image mechanical strains spatially resolved over depth and over the lateral coordinate.

As was described above, echo signals were aligned relative to the segmented contours. Strains inside the phantom were calculated analyzing two consecutive analytical echo-signal frames and the corresponding B-mode images. In Fig. 6(b) the axial strains, which were estimated using the phase-sensitive, strain-estimation approach, are shown. Only strain estimates having correlation coefficients \(\rho > 90\%\) are mapped. Pixels in the strain image corresponding to smaller correlation coefficients are marked white, because these estimates are supposed to be unreliable. Therefore, dropouts are visible in all strain images as a result of echo-signal decorrelation due to out-of-plane displacements, out of focus displacements, and speckle decorrelation. It can be seen that almost no axial elongations (positive strains \(\varepsilon_z > 0\)) or compressions (negative strains \(\varepsilon_z < 0\)) take place inside the agar, whereas the gelatin is strongly elongated in axial direction.

Axial and lateral strains, which were estimated with the speckle tracking technique described above, are shown in Fig. 6(c). The axial strain estimates are in a good agreement with the estimates in Fig. 6(b). Because the structures are considered to be almost incompressible, lateral and elevational strains occur in addition to the axial strains. In the phantom, lateral compression is observed inside the agar, which can be seen in the lateral strains image in Fig. 6(c).

The phantom measurements allow one to compare the two-strain estimation approaches. With the phase-sensitive, axial-strain estimation approach, a fraction of 26\% of the strain estimates inside the phantom was marked to be unreliable, see Fig. 6(b). In comparison, with the speckle tracking only 5.7\% of the strain estimates inside the phantom were found to be unreliable. Therefore, it
can be concluded that the speckle tracking technique is more robust against decorrelation. This finding is plausible because lateral tissue movements are tracked, and, thus, correlation is improved.

However, the spatial resolution is better for the phase-sensitive, axial-strain estimation approach than with the speckle tracking technique. Displacements are analyzed in sampling intervals equivalent to the axial and lateral window shifts, i.e., $\Delta z_{\text{shift}} = 80 \, \mu m$ and $\Delta x = 33 \, \mu m$ for the phase-sensitive, axial-strain estimation approach, and $\Delta z_{\text{shift}} = 128 \, \mu m$ and $\Delta x_{\text{shift}} = 260 \, \mu m$ for the speckle tracking. In both cases, strains are estimated as the slopes of linear regression fits over estimates in 10 adjacent windows, which, together with the window shifts, determines the resolution of the resulting strain images.

**B. Normal Skin**

The first in vivo measurements with the implemented system have been performed on normal, healthy skin. In the B-mode image in Fig. 7(a) the dermis appears as an echo-rich structure, whereas the underlying subcutaneous fat appears hypoechoic. The contour plot in Fig. 7(a) shows that the overall elevation of the skin surface is very homogeneous. Presume the skin and subcutaneous fat can be considered to be layered media in a first approximation, which is a reasonable assumption for healthy skin, the skin surface elevation in response to the applied pressure already indicates the elastic properties of the underlying tissue. Analyzing the phase-sensitive, axial-strain image in Fig. 7(b), significant axial elongations are visible at the top of the subcutaneous fat, whereas the axial strains in the dermis are small. The correlation of the analyzed echo signals in the subcutaneous fat is insufficiently low to deliver reliable axial-strain estimates because the echo signal level is too low.

In Fig. 7(c) axial and lateral strains, which were estimated using the speckle tracking approach, are shown. Again, the axial-strain estimates are in a good agreement with the estimates obtained using the phase-sensitive approach. It can be seen that mainly lateral elongations appear in the dermis.

**C. Skin Lesions**

Altered skin structures in burn scars as well as nevi were investigated. The B-mode image in Fig. 8(a) shows a burn scar on the left-hand side. In the healthy skin at the right-hand side, the dermis appears hyperechoic, whereas the echo signal level is significantly lower in the scar. Especially inside the scar, significant changes of elasticity are expected as a result of the disarranged and dysmorphic elastic and collagen fibers, which are present in burnings.

The contour plot in Fig. 8(a) already depicts a significant difference between the burn scar and the healthy skin. This also becomes apparent from a comparison with the contour plot in Fig. 7(a) for the healthy skin, for which the skin surface elevation is much more homogeneous. The axial-strain estimates, which were obtained with the two approaches, are in a good agreement with each other, see Figs. 8(b) and (c). They show significant axial elongations in the burned skin, whereas the axial strains in the healthy dermis on the right are small. At the same time, large, lateral compressions are found in the healthy skin. These findings can be explained by the disarrangement of elastic and collagen fibers, which determine the mechanical properties of the dermis [3], [40].

In Fig. 9(a) a B-mode image of the imaged nevus and the segmented contours are shown. The nevus appears as
hypoechoic structure inside the dermis. It can be seen that the skin surface elevation was very homogeneous during the echo-signal acquisitions. Again, large axial elongations occur in the subcutaneous fat, whereas the axial strains are small in the dermis, see Figs. 9(b) and (c). Inside the nevus, a significant axial compression takes place. The occurrence of compressional strains can be explained by the relatively complex mechanics and boundary conditions. The nevus is an isolated structure with different elasticity than the surrounding tissue, and both structures are connected with each other. Due to the applied suction, the nevus and the surrounding dermis are unequally drawn axially and laterally into the slot at the bottom of the applicator, resulting in local elongations and compressions.

Fig. 9(c) shows that in lateral direction mainly elongations occur. It can be concluded that the elastic properties of the nevus are significantly different than those of the surrounding dermis. In our future work, we plan to investigate the mechanical properties of skin lesions in some greater detail in order to evaluate possibilities for characterization of skin lesions based on measured strains.

IV. Discussion

In this paper, a new approach for in vivo imaging of elastic properties of skin using high-frequency ultrasound in the 20 MHz range was presented. The implemented strain imaging system is based on the acquisition of RF echo signal frames with a mechanically scanned single-element transducer, while suction at the skin surface is caused through a stepwise decrease in pressure. A computer-controlled vacuum pump system was developed to achieve well-defined and reproducible conditions during the automated measurement. Axial and lateral strains inside the skin are estimated by segmenting the skin surface, aligning the echo-signal frames relative to the segmented contours, and analyzing the displacements inside the tissue by means of a phase-sensitive, echo-signal-analysis approach and an efficient speckle tracking technique. As a result, using high-frequency ultrasound, high-resolution strain images are obtained, which depict the mechanical properties of the imaged skin structures qualitatively.

The implemented technique was successfully tested and validated with measurements on a speckle phantom. Furthermore, the potential of the developed system for in vivo applications was evaluated. It was shown that significant axial elongations occur in the subcutaneous fat and that axial strains inside the dermis are small in healthy skin, while suction is applied at the skin surface. These results are in a good agreement with the findings of Diridollou et al. [4], who concluded that the resistance to the applied vacuum is essentially due to the dermis rather than the subcutaneous fat. However, significantly large axial elongations were found in the dermis of burned skin due to the disarrangement of elastic and collagen fibers, strongly altering the elastic properties compared to healthy skin. In the imaged nevus, significantly different strains are found compared to the surrounding dermis.

V. Conclusions

HFUS can be used for high resolution imaging of mechanical strains in the skin under in vivo conditions. In contrast to the previously available tools for the assessment of elastic skin properties that perform only measurements at a single point at the skin surface, the ultrasound-based imaging concept delivers spatially resolved information.

The applied phase-sensitive axial strain estimation approach achieves a better spatial resolution compared to the proposed speckle tracking technique, because axial displacement estimations on the basis of RF echo signal analysis can be performed using smaller axial windows. But lateral displacements are not considered, and thus decorrelation, which is caused by lateral displacements, cannot be compensated. Speckle tracking, however, allows one to estimate axial and lateral displacements, i.e., a second component of the mechanical strain field is accessible. Because speckle tracking is based on the analysis of B-mode images, and thus on the echo signal intensity only, the analysis must be performed using much larger windows than with the phase-sensitive approach. Elevational strains are not considered in the two approaches presented in this paper. Considering the rotational symmetry of the sound field of the utilized focused single-element transducers, a tracking of speckle and an estimation of strain components in all three directions would be possible. For that purpose, the above described speckle tracking technique would have to be extended to three dimensions, and echo signals from adjacent imaging planes in elevational direction would have to be acquired. Doing so, the robustness of strain esti-
mutes could further be enhanced. The applied ultrasound system, however, only allows echo-signal acquisitions in a single imaging plane, performing only a single lateral scan. Furthermore, the results presented in this paper show that even a speckle-tracking technique that estimates only axial and lateral displacements yields reasonably reliable strain estimates. A basic principle of the techniques applied here is to keep the external tissue deformation sufficiently small in order to obtain moderately small strains only, which are sufficiently small to avoid decorrelation. We proposed to verify the reliability of the calculated strain estimates, analyzing the correlation coefficient of echo signals and B-mode images, compensated for estimated displacements. Furthermore, we proposed to consider positive as well as negative strains in the signal analysis in order to take elongations as well as compressions into account. For this purpose, positive and negative axial and lateral displacements, which might occur, have to be analyzed and considered.

In our future work, we will further develop the proposed strain imaging technique for applications in dermatological research and in clinical dermatology. Furthermore, we intend to use the estimated strains as input for an elastic skin model considering the given boundary conditions in order to reconstruct elastic tissue parameters, i.e., the elastic moduli. In contrast to analyses, which have already been performed by other groups, taking into account only a few measured elevations of boundaries between skin layers carried out at discrete points [5], [20], much more information can be fed into the model by using the techniques outlined above.

ACKNOWLEDGMENT

The cooperation of Sven Scharenberg, taberna pro medicum GmbH, Lüneburg, Germany, for the implementation of software modifications of the ultrasound system is greatly appreciated.

REFERENCES

Michael Vogt (S’96–M’04) was born in Hagen, Germany in 1969. He received his M.S. and Ph.D. degrees in Electrical Engineering from the Ruhr-University Bochum, Germany in 1995 and 2000, respectively. He is currently working at the Institute of High Frequency Engineering of the Ruhr-University Bochum, Germany. His research interests are high frequency electronics, medical image processing and medical ultrasonic imaging, especially high frequency ultrasound, Doppler techniques, and elasticity imaging.

Helmut Ermert (M’79–SM’98–F’00) received the Dipl.-Ing. degree in Electrical Engineering and the Dr.-Ing. degree from the Technical University (RWTH) Aachen, Germany in 1965 and 1970, respectively. In 1975 he received the Dr.-Ing. habil. degree (Habilitation) from the Engineering Faculty at the University of Erlangen-Nuremberg, Germany. From 1966 to 1970 he worked on millimeter wave and microwave engineering at the Technical University (RWTH) Aachen. From 1970 to 1975 he was involved in teaching and research in microwave integrated circuits, microwave ferrites and microwave measurement techniques at the University Erlangen-Nuremberg. From 1978 to 1987 he was a Professor of Electrical Engineering in Erlangen working on microwave and acoustic imaging using various fields and waves (ultrasound, microwaves, thermal waves, and eddy current fields) for diagnostic purposes in medicine and engineering. Since 1987 he has been Professor of Electrical Engineering and Director of the High Frequency Engineering Institute at the Ruhr-University in Bochum, Germany. He is continuing research on measurement techniques, diagnostic imaging, and sensors in the RF and microwave area as well as in the ultrasonic area for applications in medicine, nondestructive testing, and industry. In 1991 he was co-chairman of the 19th International Symposium on Acoustical Imaging in Bochum, Germany and 2001 co-chairman of the 35th Annual Biomedical Engineering Conference (BMT 2001) of the German Society of Biomedical Engineering (DGBMT/VDE) in Bochum. Since 2004 he is Director of the University Center for Medical Technology (UZMT) Bochum.

From 1989 to 1991 Dr. Ermert was an elected member of the Administrative Committee of the IEEE Ultrasonics, Ferroelectrics, and Frequency Control Society (Region 8) and since 1995 he is an Associate Editor of the IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control and of the Journal “Biomedizinische Technik” (Biomedical Engineering). He was president of the German Society of Biomedical Engineering (DGBMT, 1995–1997). In 2000 he was elected as a Fellow of the IEEE. He is also the speaker and coordinator of a Center of Excellence for Biomedical Engineering (KMR) in Bochum, which is supported by the Government of the Federal Republic of Germany. In 2001 Dr. Ermert was elected as a member of the Academy of Science of North-Rhine-Westphalia, Dusseldorf, Germany and an honorary member of DGBMT (VDE).