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Acousto-mechanical behaviour of ex-vivo skin: Nonlinear and viscoelastic properties

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ABSTRACT

The mechanical behaviour of skin is significant for some applications including dermatology, surgery, and impact biomechanics science. In this work, we have investigated the study of the acousto-mechanical viscoelastic properties of skin. For that, both tensile-relaxation and ultrasonic tests were conducted on porcine tissue samples in fibre directions. To understand the complex skin aging phenomena, we used strength tensile test correlated with the Nonlinear Time Reversal signal processing tool extension "TR-NEWS". Uniaxial tensile tests were carried out at a strain rate of $5 \cdot 10^{-3}$ mm s^{-1} on skin using a load-relaxation-discharge load path with increasing amplitude and offset. This work is also under way to extend the frequency range of ultrasounds to 50 MHz. Digital Image Correlation was used for 2D strain measurement of the dermis. From this analysis, we conclude that fresh porcine skin should be modelled as a nonlinear viscoelastic material with strain-rate dependence. The obtained hysteresis loop shall be taken as significant skin damage.

1. Introduction

Skin is a living complex tissue which contains heterogeneous layer: epidermis, dermis, and hypodermis. The epidermis consists of cells and cellular debris, the dermis consists of mostly networks of fibrous protein collagen, with interspersed elastin, and reticulin [1], and the hypodermis is principally made up of connective tissue and fat lobules. Collagen fibers account for 75% of the dry weight of the dermal tissue [2]. The damage to these fibers is responsible for skin aging. Previous studies suggested that the deformation characteristics of skin are very complex [3,4]. The skin tissue is an anisotropic, nonlinear, viscoelastic material under little incompressible deformation [5].

Skin anisotropicity was recognized by Langer, who mapped the natural lines of tension that occur within the skin [6]. These lines are known as the Langer lines. A tensile test showed that the mechanical deformation of skin is dependent upon the specimen's orientation along Langer lines [7]. Most recent studies have used optical coherence in vivo images to indicate a large difference between the Young moduli of skin along the parallel and orthogonal directions of the Langer lines [8].

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J. Benítez and F.J. Montáns have established an anisotropic model to describe the mechanical properties of human skin in uniaxial tension along load axes in the 0°, 45°, and 90° directions [9]. Groves et al. [10] developed ex vivo tests on circular samples of both murine and human skin. These tests are considered as significant because they were achieved in different directions for the same specimen to study the anisotropic behaviour of skin and were numerically analyzed in [11].

A stress–strain skin characteristic of some previous works displays nonlinear behaviour and describes the response of skin to deformation [12–14]. According to these studies, in the loading phase, skin is very compliant and large deformations occur for relatively low applied loads. At this stage, the fibers are largely unaligned. Afterward, skin stiffness progressively increases as the fibers align themselves under the load applied. The stiffness of skin increases continuously, rapidly, and linearly until the collagen fibers become mostly aligned. At this stage, the overall mechanical response becomes dependent on the mechanical properties of the collagen fibers, which are stiffer than those of elastin. As was reported by some authors [15,16], the directional bias of collagen distribution is responsible for the anisotropic behaviour of skin. The Young modulus of collagen is about 1.0–10 GPa. Furthermore, the modulus of elastin is about 100 kPa, i.e. several orders of magnitude less than that of collagen [17]. Elastin accounts for 4% of the dermis volume and is presented as thin strand attached to the collagen fibers [15]. Elastin and collagen are cross-linked to hyaluronic acid embedded in the ground substance's amorphous material, a very viscous, thixotropic semi-fluid [18].

Several works were focused on the determination of the viscous mechanical behaviour of skin. The rheological properties are physiologically based, primarily, on the previously mentioned viscous nature of the matrix and also on its interaction with the fibers, as well as on the inter-fiber extensions [19].

The viscoelasticity of skin is dependent on strain level, rate, and temperature [20]. A strain-level dependence of relaxation functions is found in some biological tissues such as skin [18]. Anisotropy also plays an interesting role in the viscoelastic properties of skin [21]. Viscoelastic behaviour in skin at small deformation levels is frequently measured through dynamic methods like wave propagation, permitting also an anisotropy analysis [22]. As was suggested by previous authors [23,24], the main contributors to the viscoelastic behaviour of skin are the collagen fibers and the interaction between collagen and matrix.

In this study, we provide new experimental data about ex-vitro porcine skin, focusing, in particular, on the viscoelastic and anisotropic properties of skin. We also correlated the typical uniaxial tensile tests with classical medical ultrasonic imaging or Non-Destructive Testing (NDT) to quantify the skin deformation degrees and to understand the complex mechanical properties of soft tissues.

Although some recent researches on the mechanical properties of skin report in vitro and in vivo experiments [25,26], there are only very limited works concerning the deformation cycle allowing one to evaluate the viscoelasticity behaviour of skin using synchronization with a novel setup for mechanical loading and ultrasonic measurements.

In this work, we have limited our experiments to in vitro uniaxial tensile tests. It was decided to perform in vitro tensile tests with porcine tissues for two important reasons. Primarily, this test provides simple stress–strain relationships that can be easily modelled and quantified with boundary conditions that are well defined. Secondly, in this work the further dynamic response until fatigue and failure is tested. Many in vitro studies use human skin substitutes such as silicone or polyurethane [27,28] and in vitro tests on natural soft skin tissue are mainly limited. This study aims to provide new material data for porcine skin which can be applied to constitutive models in a number of technical areas such as cosmetics, surgical simulation, forensic pathology, and impact biomechanics. Simple tension tests remain important because they serve to evaluate the level of anisotropy. However, uniaxial tensile tests alone are not enough to determine multi-dimensional material models for soft tissues. To understand this complex mechanical property and the memory effects that are responsible for the materials' aging, classical medical ultrasonic imaging or Non-Destructive Testing (NDT) was investigated.

Multi-modal based imaging approaches have the potential to image such nonlinear information as already established in NDT. The nonlinear signature of aging has been measured recently in several experiments and configurations [29]. Time Reversal (TR)-based NEWS (Nonlinear Elastic Wave Spectroscopy) methods have the potential to become powerful and promising tools for the NDT industry [30]. The systemic approach of the TR-NEWS ultrasonic complexity is unclear generated innovation for medical applications with extended experimental results developed for echo-dentography on human teeth [31] or to locate and destroy a kidney stone in the body during lithotripsy treatment [32–34]. Some studies include a nonlinear analysis of hysteretic behaviour. The association between TR-NEWS and MTS loading set-ups enables to measure the nonlinearity of porcine skin. Digital Image Correlation (DIC) is used to evaluate the deformation field of the longitudinal and transversal strain directions. The repeatable measurement results presented in this work show a progressive deterioration of the mechanical properties, confirmed by the increasing number of hysteresis cycles, which are followed by relaxation.

The objective aim of this paper is to provide an acousto-mechanical method for measuring the elasticity, viscoelasticity, and relaxation parameters of an in vitro skin sample.

2. Materials and methods

2.1. Specimen preparation

The used porcine skin is obtained from the abdomen area of the same domestic pig. Five skin samples were excised from same subject. with a scalpel and cut into a rectangular shape in the direction of the skin fibers.

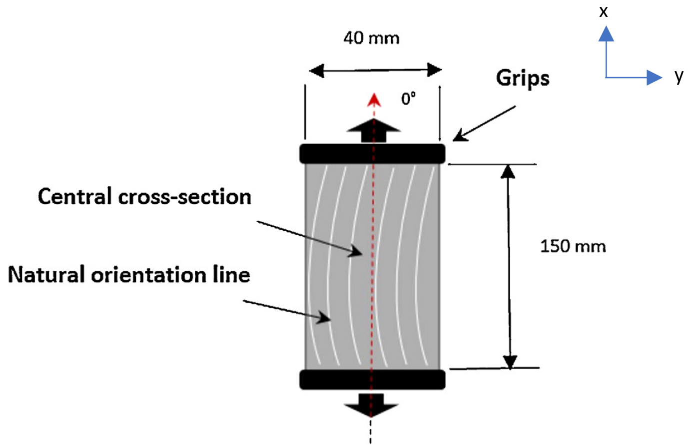

Fig. 1. Posterior porcine skin in uniaxial tension along a loading axis at 0° with respect to Langer's natural lines.

The adipose tissue of each specimen was then carefully removed using a scalpel. The thickness of skin after removal of adipose tissue was measured to be between 3 and 4 ± 0.2 mm. The dimensions of the test posterior samples were measured before excision. All samples are 150 × 40 × 3 mm in size. A total of three specimens were tested successfully. In accordance with Eshel and Lanir's study [35], the used skins were therefore not pre-conditioned prior to testing.

Fig. 1 gives the orientation details of the loading axes used during the tensile tests, common for posterior specimens from porcine skin.

2.2. Tensile tests

The tensile tests, performed at 0° with respect to Langer's natural lines, were achieved using a universal tensile test machine "An Instron 8800". The samples were clamped using specially designed anti-slip clamps to counteract the tendency of samples to slip in ordinary grips. The velocity of the crosshead was 0.5 mm/s. A 500-N load cell was used to measure displacement and tensile load. Except for the first cycle, the loading starts whenever a zero force level is reached during unloading. It is noted that all the tests performed on the various samples were completed within 3 h to ensure the freshness of the skin tissue. The load was set to 0 before starting the test. The strain rate was applied for the loading and unloading steps. The loading steps are performed until a constant maximum imposed strain rate (10%) is reached. The strain rates and the displacements are directly imposed through the machine's crosshead. The samples were clamped using special anti-slip clamps. The velocity of the crosshead was 0.5 mm/s. The results are obtained in terms of force–displacement. The nominal stress P and the engineering uniaxial strain ε are given by the relations

$$P = F/S_0(1)$$
$$\varepsilon = (D\, D_0)/D_0 \tag{1}$$

where F is the applied force and S_0 is the initial area of the cross section of the skin samples, D and D_0 are the current and initial lengths of the sample.

Each tensile test was recorded with a digital video camera to record any irregular behaviour during the tensile test and for the following use of DIC. The gauge length and width were both measured optically.

The main focus of this work is an investigation of the hyperplastic properties of skin. Further creep and stress relaxation tests, requiring additional skin samples, would need to be approved to characterize the viscoelasticity of skin.

2.3. Digital image correlation

The mechanical characterization is carried out during the experiments using DIC. The stretch ratio was calculated via the displacement cell attached to the cross-head of the tensile machine and it was also calculated via DIC. It is a full-field optical strain measurement method using image registration to measure the 2D or 3D material deformations. These correlations are based on images taken with an IDS video camera (1:2.8 50 mm 30.5 TAMRON lens). Black spray paint was applied to the skin surface to generate the desired random speckled pattern necessary for the correlation.

2.4. TR-NEWS signal processing

An advanced signal processing technique based on multi-scale analysis and multimodal imaging was investigated. The Nonlinear Time Reversal method was used, in this work, to detect the structural damages in the complex medium.

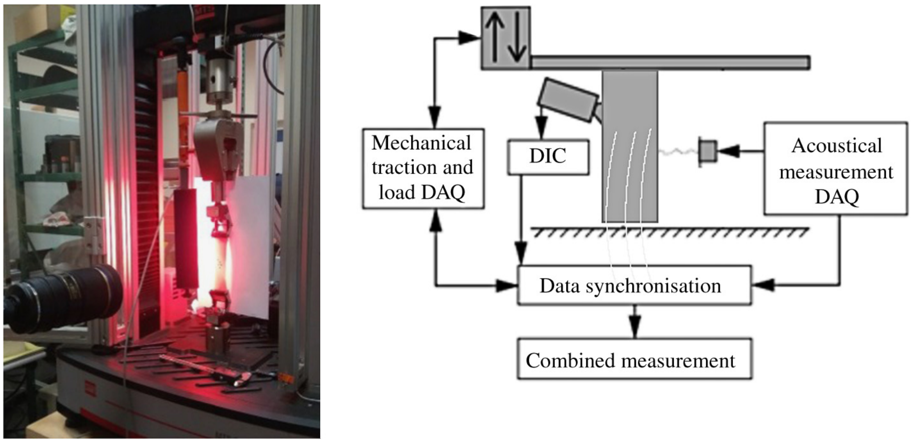

Fig. 2. The synchronization diagram of ultrasonic and mechanical measurements on the porcine skin using DIC.

The TR-NEWS signal processing approach, which is used here, consists of the following signal processing steps: chirp broadcasting, reception, correlation, time reversal, rebroadcasting, and return reception. Such signal processing allows us to better understand the physical meaning of the cross-correlation function of a complex material. Indeed, the TR-NEWS signal approach coming from nonlinear effects would be measured by the symmetry's fields. The devices used for implementing the process are calibrated and related to pulse excitations that allow us to detect the nonlinear break behaviour of the porcine skin. The TR-NEWS Data Acquisition (DAQ) system was designed by Juvitek (TRA-02 "0.02–5 MHz"). The synchronization and amplification were performed using an amplifier ENI model A150 (55 dB at 0.3 35 MHz) and a pulse generator (GPG-8018G) as a pulse extender.

Two sensor types were chosen in this work: the shear wave transducer (ABFP-0202-70 "2.25 MHz") for wave emission and the longitudinal transducer (V155 "5 MHz") for wave reception. An ultrasonic transducer is attached to each skin sample by a hand clamp as presented in Fig. 2. In addition, elastic waves guided periodically at specifiable time intervals and emitted by an actuator or ultrasonic transducer are detected by sensors or ultrasonic transducers and examined for changes in the emitted waves. The TR-NEWS measurement, which is counted accordingly by the load frame, is controlled by specific software.

3. Results and discussion

3.1. Uniaxial tensile tests

Some basic biomechanical properties are first investigated by uniaxial tests, which are very useful for understanding the ratcheting behaviour more deeply. The obtained experimental results are shown in Fig. 3.

For each tensile test performed, a stress–deformation curve and a strain–time curve were obtained. The nominal stress was then calculated by dividing the force by the undeformed cross-sectional area of the samples. The stretch ratio was calculated by dividing the current length of the specimen by its initial length. In this way, nominal stress vs stretch ratio graphs were plotted for each specimen. A characteristic number of these curves were identified as descriptive parameters. Fig. 3(a) illustrates the hyperplastic behaviour obtained in the tension test. The stress–strain response of porcine skin is extremely nonlinear, and the tensile stress–strain curve can be separated into three parts: the first part with an increased tangent modulus, the second part with a constant tangent modulus, and the third part with a decreased tangent modulus. The same phenomenon has been obtained and commented by Fung et al. [36]. One can also see that the biomechanical response of porcine skin is anisotropic in both directions. The mean value of the instantaneous initial Young modulus in tension of the porcine skin E_0 in the parallel direction of the uniaxial tensile test is evaluated as $E_0 = 0.35 \pm 0.2$ MPa, whereas the initial Young modulus E_0 in the orthogonal direction is evaluated as $E_0 = 2.1 \pm 0.4$ MPa. Thus, we notice that the instantaneous initial Young modulus is significantly higher for a fresh tissue in cross fiber directions. This is in total agreement with the findings of some previous studies [8,37], where a large difference between the Young moduli of skin along parallel and orthogonal directions to natural lines has been clearly demonstrated. Indeed, it has been suggested that the deformation responses of skin are dependent upon the specimen's orientation.

An illustrative viscoelastic behaviour through tension tests is displayed in Fig. 3(b). A relative deformation–time curve is examined, as well as the initial axial strain value produced at the moment when the prescribed peak force is reached in the test. It appears that the deformation in parallel of the along natural lines of the porcine skin increases with the testing time, while the deformation in orthogonal direction decreases with time. These findings are consistent with the incompressibility theory of biological tissues. The Poisson ratio is determined in the x–y plane as shown as Fig. 1. The mean Poisson ratio is evaluated as 0.51 ± 0.12.

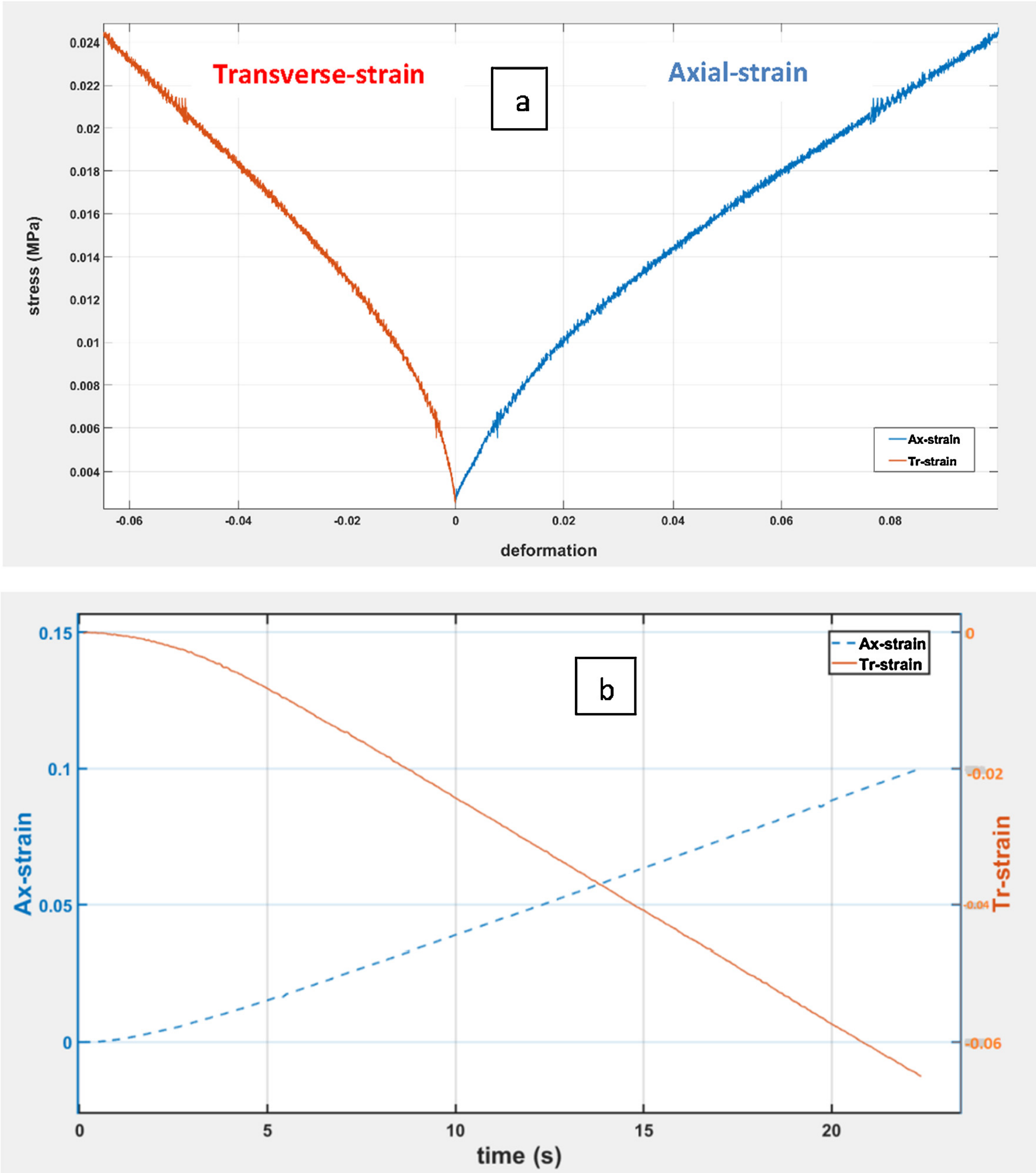

Fig. 3. Typical stress–deformation graph for the experiments. The initial elastic modulus is defined as the slope of the linear portion of the curve (a). Typical axial strain–time and transverse strain–time curves (b) of porcine skin.

3.2. Cyclic tension tests

Five-nominal force-displacement cyclic tests, using loading–unloading and relaxation time “25 s”, were performed on the porcine skin samples in the orthogonal direction. The obtained experimental results are shown in Fig. 4. It appears that the relative peak and valley strains increase progressively with increasing the number of cycles (Fig. 4a). This result seems similar to those from some previous research that used a stress-controlled cyclic loading method [38,39].

The ratcheting strain increases with the increasing mean force and time, as shown in Fig. 4(b). When the loading level is high and after the first cycle, the ratcheting ax-strain rate continues to increase until the relaxation-imposed time (25 s), and then decreases. The experimental cycle tensile results in function time illustrative viscoelastic behaviour of the porcine skin. The above-mentioned experimental observation shows that ratcheting also occurs for the porcine skin at room temperature when the skin samples are subjected to cyclic tension unloading, as well as to cyclic loading–unloading tests. However, the

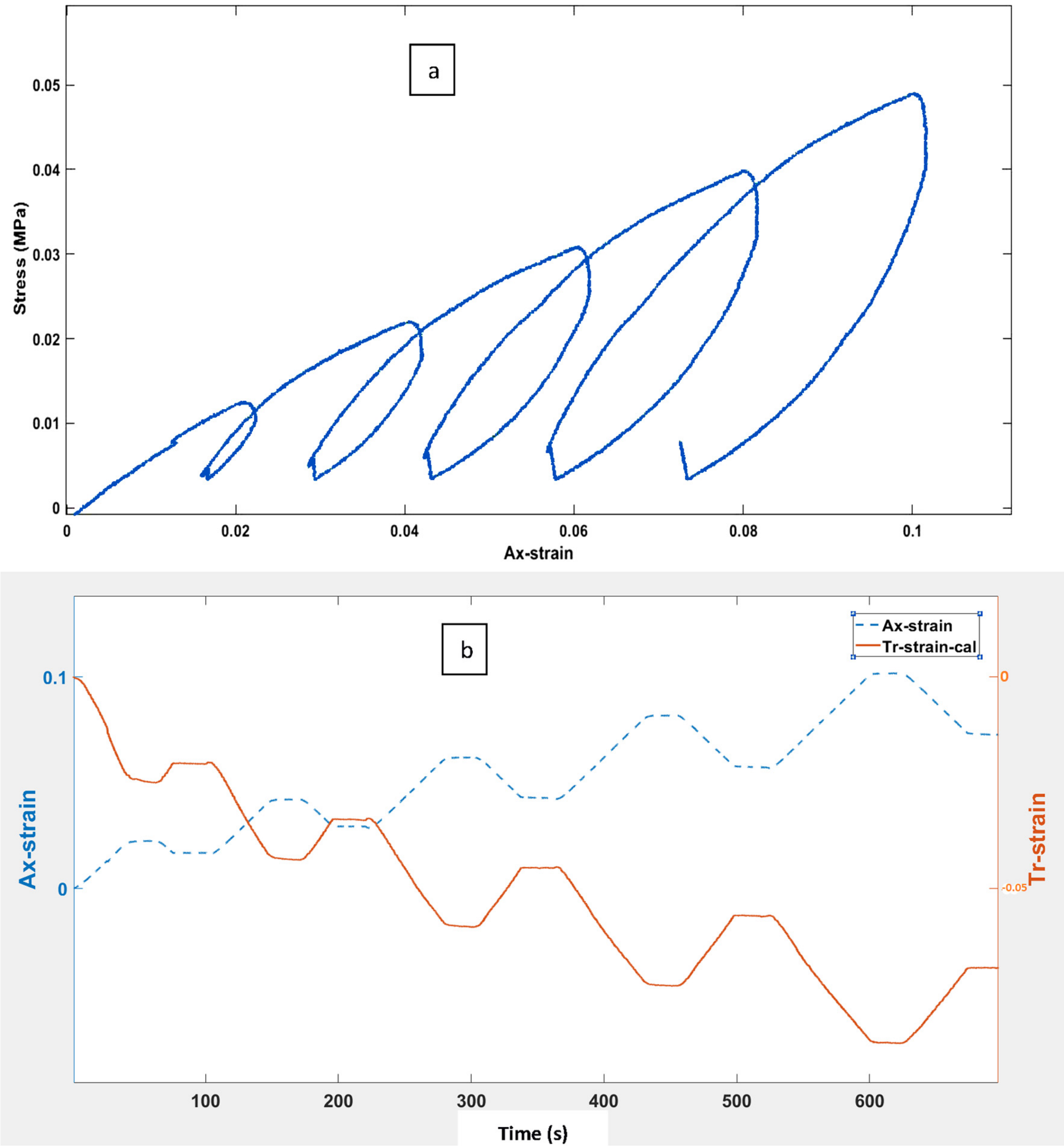

Fig. 4. Cycle tensile stress–strain curves (a); axial (Ax) and transverse (Tr) strain–time curves (b) testing on porcine skin during five loading cycles.

porcine skin tissue has a different physical mechanism. The ratcheting of the porcine skin is mainly caused by its remarkable viscosity, which has been demonstrated clearly by the tensile tests at different loading rates by Kang et al. [40].

The initial Young modulus of each cycle was determined from the elastic part of the cyclic loading–unloading curves. The obtained results are presented in Fig. 5. One can see that the initial Young modulus increases progressively with increasing the stress rates. It may be explained that the collagen fibers are reoriented in the direction of the applied normal tension force and regenerate the structure and increase the mechanical strength. According to several papers [41], the dermis, which acts as a support tissue, is responsible for skin's resistance. When viewed from its ultra-structure, the dermis is structured as a complex 3D network of collagen, elastin, and reticulin fibers that are immersed in a semi-liquid called "fundamental substance". Mechanically, the fundamental substance is a viscous gel. In vitro tests have shown that collagen fibers are highly resistant, while elastin fibers have high extensibility [24]. Several studies have shown that collagen fibers are oriented in the stress direction according to the three uniaxial traction phases. Kang and al. [40] based their findings on the microscopic observation of the collagen fiber bundles and on their variation during the monotonic tensile test. They concluded that such viscoelastic performance is satisfied only within a certain applied load.

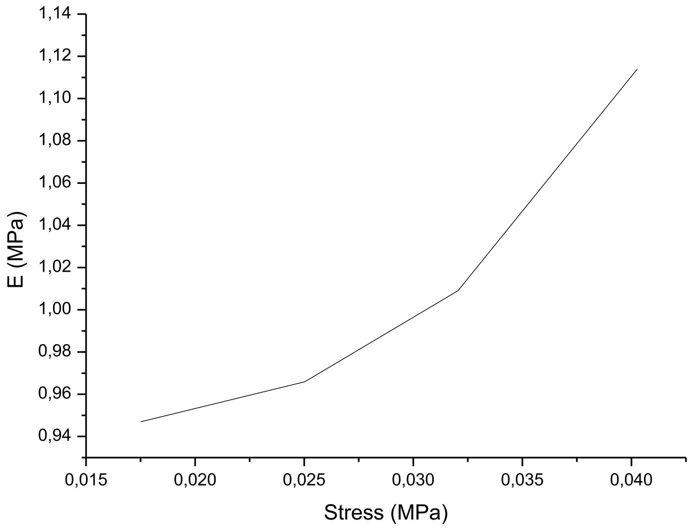

Fig. 5. Evolution of the initial Young modulus as a function of the tensile stress applied to porcine skin.

Skin is a highly nonlinear, anisotropic, viscoelastic and nearly incompressible material. A typical stress–stretch graph for skin exhibits non-linear behaviour, and its response is generally described as a three-phase one [41]. In the initial loading phase, skin is very compliant and large deformation occurs at a relatively low applied load. In this phase, the fibers are largely unaligned. In the second phase, the stiffness of skin gradually increases as the fibers align themselves in the direction of the applied load. The third phase is an almost linear phase where stiffness increases rapidly as the collagen fibers are mostly aligned and the overall mechanical response becomes dependent on the mechanical properties of the collagen fibers, which are stiffer than elastin by three grades of magnitude.

In the literature, depending on the experimental conditions, the Young modulus of skin varies between 0.42 MPa and 0.85 MPa for torsion tests [40], 4.6 MPa and 20 MPa for tensile tests [41]. In our case, after tensile tests, the Young modulus was smaller than the one found in the literature. The main differences of these methods are that they modify the natural properties of skin and the experimental variables during the test. Therefore, the measured values of mechanical characteristics could be affected, so they might not be accurate.

It is known that the soft tissue of skin is a typical viscoelastic material, and the residual strain after loading–unloading tests will be reversible after a certain recovery time. Porcine skin is anisotropic, the bi-axial and multi-axial cyclic tests are necessary to understand the behaviour of skin's soft tissue more deeply. This work is currently in progress and will be discussed in a future work.

3.3. Acousto-mechanical behaviour

An arbitrary load path is imported into the load frame controller. The load frame excitation will start after the first full TR-NEWS measurement. Then, it follows the given path, stopping for the duration of each new TR-NEWS test, which is automated. Nineteen TR-NEWS measurements were taken at different strain and stress. These obtained measurement points can be seen in Fig. 6. In this test, the starting values of extension and load are non-zero. Fig. 7 shows the TR-NEWS focusing measurements at different load and strain values. Nineteen TR-NEWS measurements are captured and used to evaluate the acousto-mechanical responses of skin. The experimental results show that the TR-NEWS response of porcine skin, at the start of the test, is increasing with load, while the last measurement has the highest load and strain rates.

As was shown by previous authors, the strain increase with increasing load can be explained by the damage or aging behaviour of the skin. The TR-NEWS focusing measurements at increasing strain shown in Fig. 7 exhibit increasing side lobe amplitude of the TR-NEWS response with increasing strain. This can be linked to increasing damage to skin [42,43], as differences are small but sure, and many experiments have been performed to confirm this behaviour [44].

4. Conclusion

Experimental uniaxial tensile tests of posterior porcine skin, only at 0° with respect to Langer's natural lines, recorded with a video camera, were conducted to study the ratcheting behaviour. However, in order to fully characterize the mechanical behaviour of porcine skin under impact, its viscoelastic properties must also be determined. The cyclic tension–unloading tests should be studied. A higher loading rate increases the produced strain in the cyclic test. It has been shown that skin soft tissue is a typical viscoelastic material and that porcine skin strain could recover completely after unloading and re-

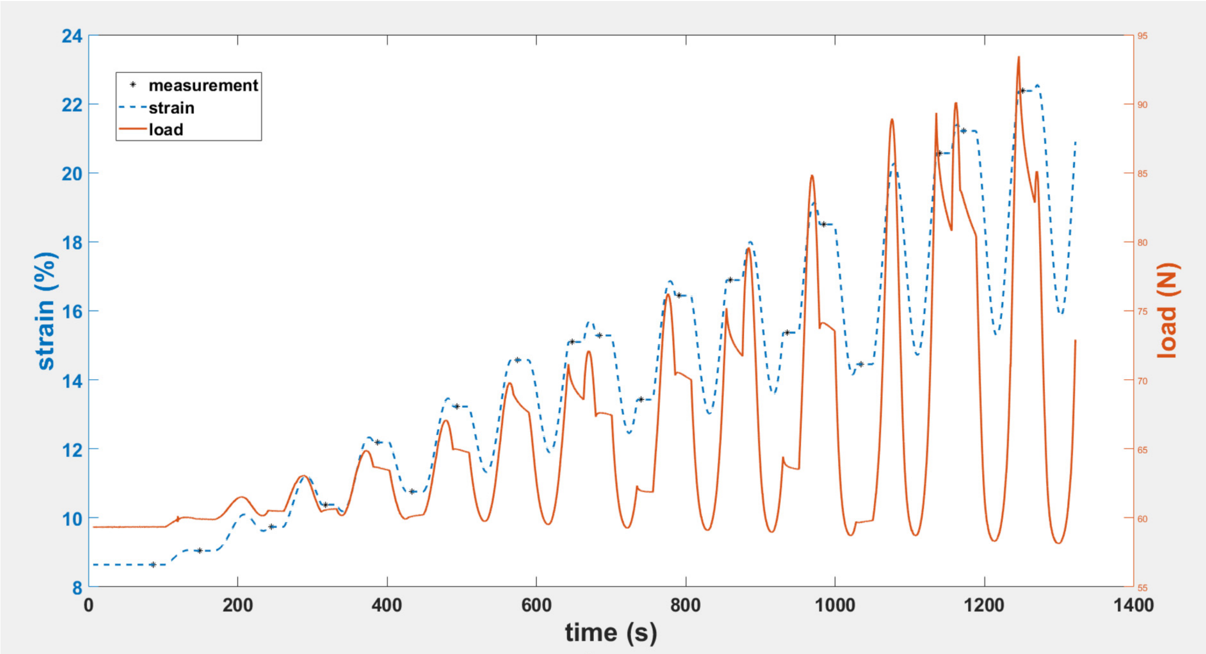

Fig. 6. Synchronization of the strain and the load as a function of time with TR-NEWS measurement points on porcine skin.

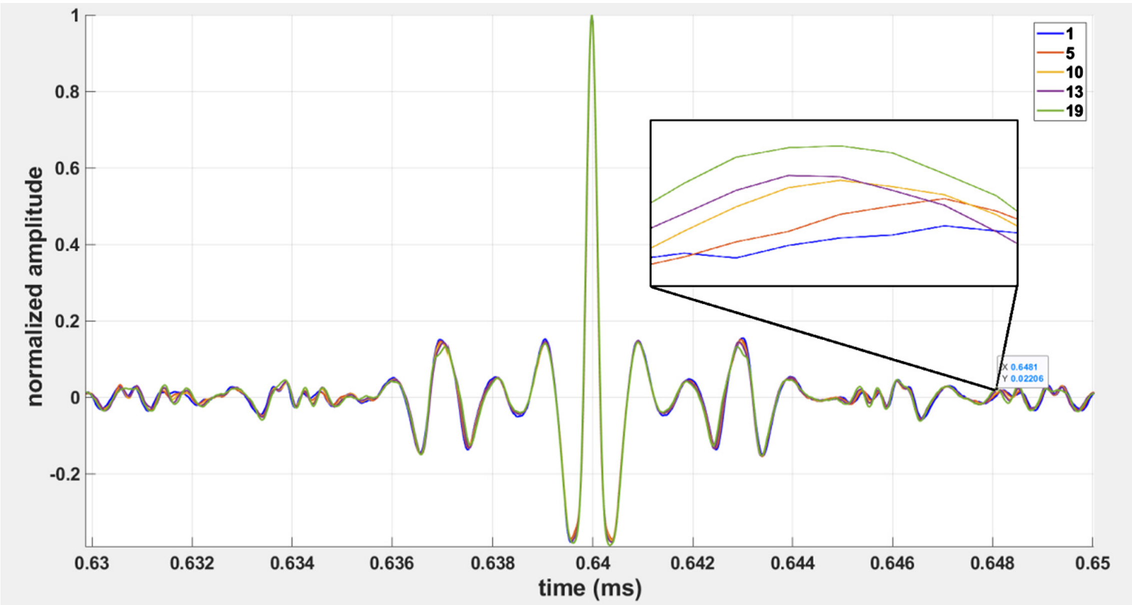

Fig. 7. TR-NEWS focusing measurements.

laxation, because many collagen fibers of porcine skin are mostly aligned towards the direction of stress. These fibers are probably responsible for the overall mechanical response.

Acousto-mechanical testing setup, a novel fully synchronized method, has been also presented in this paper. It unites the data from load frame extension path, load measurements, video extension measurements for determining actual strain and modern ultrasonic nonlinear testing methods. This setup allows measuring the nonlinearity, hysteresis, ageing and other complex multiscale mechanical properties of the test sample in an automatic way.

One of the important challenges of our research will be to relate the data obtained on animal skin to the properties of human skin. Due to the difficulty to obtain human tissues, ex vivo tests using a new approach could have a significant impact in many fields, especially in the medical and cosmetic domains.

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