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Mechanical and topographical anisotropy for human skin: Ageing effect

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A B S T R A C T

Skin ageing is a complex process which strongly impacts the three skin layers (epidermis, dermis, hypodermis) both functionally and structurally. Of particular interest are the effects of ageing on the dermis biomechanics and how this evolution can impact the reorganization of the cutaneous lines which compose the skin relief. It has been argued that the skin relief could reflect the underlying mechanical condition of the skin. Nevertheless, there is not yet conclusive evidence of the existence of such a link.

This work aims at experimentally studying, *in vivo*, the correlation between the anisotropy of human skin biomechanics and skin topography as a function of ageing.

The study was conducted on a panel of 20 men divided into 4 groups according to age (from 23 to 64 years old). The measurements were performed on the right volar forearm of each volunteer.

For the biomechanical measurements, an innovative contactless bio-rheometer was developed. It allows access to the mechanical behaviour of the skin in several directions. This device generates an air blast without any contact with the skin area and measures its dynamic response (evaluation of speed of wave propagation) with a linear laser. Moreover, a turntable enables measurements to be made in different angular directions.

To analyse the topography of skin relief, we proposed a new method, based on watershed and linear radon transformations. First, an optical analysis of a replica of the skin relief is performed. Then, from the skin image obtained, the density of the cutaneous lines is calculated in different directions using watershed transformation. The orientation of the detected lines is then estimated with an algorithm based on linear radon transformation.

The results observed show a good correlation between the skin relief and the mechanical properties of the skin all along the ageing process. For both topography and mechanical properties, there is a transition from an almost isotropic mechanical behaviour to an anisotropic one as a function of ageing process. Thus, we might conclude that the skin relief reflects the underlying mechanical conditions of the skin.

1. Introduction

Human skin is a heterogeneous and anisotropic living material. It is composed of three different layers from the inner to the outer: hypodermis, dermis and epidermis. The hypodermis consists primarily of loose connective tissue and lobules of fat. The dermis consists of a network of collagen and elastic fibres, blood vessels and lymphatic elements. The elastic fibres are responsible for the skin elasticity and the collagen fibres, the most abundant protein in the human body, act on its resistance (Silver et al., 2001). These fibres are immersed in an interstitial fluid composed of proteoglycans, ions and water. This layer confers to skin the main part of its mechanical behaviour. Finally, the epidermis is the layer that protects the body from dehydration and pathogens intrusions. It consists of a cohesive and stratified structure resulting from the differentiation of keratinocytes from the basal layer to the *stratum corneum* (Koster and Roop, 2007). On its surface, the skin has a specific topography depending on the anatomical site and age (Pailler Mattei et al., 2013). Microscopic observations have shown that

cutaneous surface presents a network of lines whose organisation should reflect the multidirectional tensions of elastic and collagen fibres in the papillary dermis (Zahouani and Vargiolu, 2004).

From a mechanical point of view, the human skin is a very complex structure, whose the mechanical behaviour depends on the environmental conditions, the gender and the ageing (Grahame and Holt, 1969) (Cua et al., 1990) (Auriol et al., 1993). Because of its anisotropic specific structure, human skin mechanical properties are highly directional-dependent. One of the earliest identifications of these intrinsic mechanical properties is the Langer's lines, which revealed the mechanical anisotropic behaviour of the human skin (Cua et al., 1990) (Auriol et al., 1993) (Jones, 1941) (Wong et al., 2011) (Yazdani et al., 2014). The orientation of these lines coincided with the dominant axis of mechanical tension in the skin (Pawlaczyk et al., 2013).

With ageing, skin's mechanical properties are highly altered: the skin becomes less tense and less flexible (Pawlaczyk et al., 2013). These mechanical changes also affect the skin surface topography. Pailler Mattei et al. (2013) (Pailler Mattei et al., 2013) compared *in vivo*

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mechanical measurements and topographical observations from normal skin ageing and pathologic skin ageing type cutis laxa. They suggested that the skin relief could reflect the underlying mechanical condition of the skin. Nevertheless, the mechanical measurements were performed with classical indentation tests, which did not give access to the intrinsic mechanical anisotropy of the skin.

This paper aims to study, *in vivo*, the anisotropy of human skin mechanical properties and the skin topographical properties as a function of the ageing effect. First of all, a specific air blast system device was developed to study the mechanical behaviour of the skin in several directions. Then, skin relief was assessed by a topographical analysis of skin replicas by interferometry and analysed with watershed transformation. Finally, the multi-directional mechanical behaviour of skin as function of ageing versus the skin topography was studied.

2. Material and methods

2.1. Volunteers

A total of 20 healthy Caucasian men were divided into 4 groups according to age (5 volunteers per group): G1, 26 ± 3 years; G2, 35 ± 3 years; G3, 45 ± 2 years; G4, 58 ± 6 years. The measurements were performed on the right inner forearm because the skin area is easily accessible, relatively flat and has low pilosity. No cream or cosmetic were applied to the forearm during the 24 h preceding the tests. All the volunteers were chosen with approximately the same hydration level to avoid variations due to the hydration effect on the mechanical and the topographical properties. The hydration level measured using Corneometer CM 825 (Courage – Khazaka Electronic, Köln), was around 34 ± 3 . All the subjects gave their informed consent (release signed) for this non-invasive study.

2.2. Contactless compression device

A specific contactless compression system has been developed to measure the biomechanical properties of biological tissues. This device is inspired by a previous device developed in our laboratory (Boyer et al., 2011). The test consists of blowing air onto the skin surface and measuring its dynamic response with a linear laser (Keyence 7020). This original method allowed observing the real free return of skin without any outside influence and avoiding the adhesion effect previously noticed for human skin (Pailler Mattei et al., 2004).

A schematic representation of the contactless compression device is presented in Fig. 1(a). An air compressor and a pressure regulator were used to provide a controlled air flow. The air flow output duration was

regulated by solenoid valves. The air passed through a glass pipette with an inner diameter of 1 mm. The distance between the exit of the pipette and the skin surface was optimized to 10 mm. A linear laser was used to measure the vertical displacement of the skin during the test with a sampling frequency of 8 kHz, as shown in Fig. 1(b). The laser line was composed of 800 sensors over a length of 7 mm. Finally, a turntable was placed on the head of the laser to rotate both the laser and the glass pipette together around the pipette axis. The turntable permitted to perform the measurements in different directions (angular orientation) and in the tangent plane of the skin surface (Fig. 1(b)). A software application was developed using Labview™ language (National Instruments) to control the system. For each impact test, the air flux pressure was set to 1 bar for 4 ms and 3 tests were performed for each measurement.

2.3. Confocal chromatic imaging

The skin relief measurement is obtained by an indirect method. First of all, a liquid elastomer used for medical applications (Silflo®, Flexico Ltd, UK) mixed with a catalyst is spread onto the skin surface. After few minutes the elastomer hardens and the negative of the skin relief is then obtained. An optical analysis of the negative elastomer of the skin relief, with a white light interferometric device is obtained by the positive image of the cutaneous relief (Adi et al., 2008) (Pecheva et al., 2007). The resulting skin 3D-surface image is digitally analysed and characterised with Toposurf® software.

From the skin 3D-surface image, the density of the cutaneous lines is calculated in different directions using watershed transformation (Mezghani, 2005). A watershed is a transformation defined on a gray-scale image. The watershed transformation treats the target image like a topographic map, with the brightness of each point representing its height, and finds the lines that run along the tops of ridges (Ruparelia, 2012).

The orientation of the detected lines had been estimated with an algorithm based on linear radon transformation (Jafari-Khouzani and Soltanian-Zadeh, 2005). The Radon transform is a set of line integrals that computes the projection sum of image intensities along a set of parallel lines oriented at different angles.

For this study, we estimated the density of the detected lines in different ranges of angles: every 45° angles, for 0° – 315° .

2.4. Statistical analyses

MATLAB software was used for statistical data analysis. The data are considered statistically significant if the p-value is lower than the

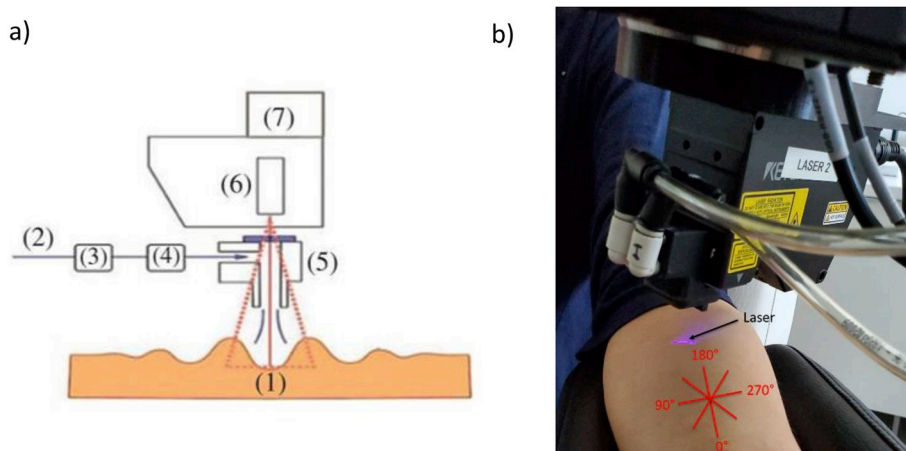


Fig. 1. Contactless indentation concept. (a) Principle of the contactless indentation system; (1) skin, (2) air compressor, (3) pressure regulator, (4) solenoid valve, (5) glass pipette, (6) 2D linear laser, (7) turntable. (b) Photograph of the system and the predetermined directions for studying the anisotropy of mechanical properties.

significance level defined (0.05 in our case). In our study, we used ANOVA to see whether we had statistically significant differences as a function of age and directions of measurement.

Spearman correlation analyses were conducted to check whether the mechanical properties of the skin correlated to the topographical ones. The Spearman's rank correlation coefficient is a nonparametric measure of statistical dependence between two variables. It assesses how well the relationship between two variables can be described using a monotonic function. A correlation coefficient higher than 0.8 indicates a strong positive correlation while a correlation lower than -0.8 a negative one.

3. Results and discussion

In the first part, mechanical properties of skin and skin topography were studied for the G1 group only, which avoids taking into account the ageing effect. In the second part, the ageing effect on skin mechanical properties and skin topography was analysed for the groups G2, G3 and G4.

1. Analysis of skin mechanical properties and skin topography

A typical response of skin surface subjected to an impact test is presented in Fig. 2. The air blast led to a local deformation of the skin and created a shear wave at its surface. The velocity of the shear wave V was calculated as:

$$V = \frac{d}{t} \quad (1)$$

where d is the distance between the sensors of the laser line (sensor positions) and t is the corresponding time. The main peak deformation was used to calculate the time delay.

Fig. 3 highlights the speed of wave propagation for the forearm measured in eight predefined directions (as mentioned in Fig. 1(b)) for the group G1. Globally, no significant difference of speed can be observed between the different directions, which is confirmed by the statistical analysis (p-value is equal to 0.79). Therefore, for the group G1, skin mechanical properties of the forearm seem to be quasi-isotropic.

For some directions, big standard deviations up to 24% (315° direction) can be noticed, which could reasonably be attributed to intrinsic features of the volunteers (sport experience, food, genetic factors, stress ...), as already described in the literature (Borges, 1984) (Zahouani et al., 2011).

As the mechanical properties of human skin are usually studied through the evaluation of its Young's modulus, the following relation, valid for an isotropic homogenous material, has been used to estimate the skin Young's modulus from the cutaneous speed wave propagation V (Lee et al., 1993) (Schneider and Schwarz, 1997) (Li et al., 2013):

$$V = \frac{0.87 + 1.12\vartheta}{1 + \vartheta} \left(\frac{E}{2\rho(1 + \vartheta)} \right)^{1/2} \quad (2)$$

where E is the skin Young's modulus, ϑ is the skin Poisson's ratio and ρ is the skin density (Li et al., 2013).

Skin is a heterogeneous multi-layer medium. So, in order to consolidate the hypothesis of elastic behaviour for skin, the measurement of the force generated by air flow on the skin surface has been performed thanks to a piezoelectric sensor. For an air pressure fixed to 1 bar, we measured a force of 15 mN applied onto the skin surface. This applied force is quite low and similar to the indentation force used in the literature for human skin (Pailler-Mattei et al., 2008). Indeed, (Pailler-Mattei et al., 2008) performed indentation tests on the forearm with a normal load of 20 mN. They showed that human skin could be considered to be mainly an elastic material. Thus, for our study, it could be assumed that the skin behaviour was rather close to the one of an elastic material. This hypothesis is supported by the calculation of the Deborah number, $D_e = \frac{t}{\tau_e}$, where τ_r is the skin intrinsic relaxation time and τ_e is the time observation. In this experiment, the relaxation time of the skin is around 200 ms and the time scale of the experiment is 1500 ms, so the Deborah number is around 0.13, which confirms that the skin behaviour could be supposed, as a first approximation as essentially elastic. Therefore, equation (2) can be used to calculate the skin Young's modulus from the skin wave velocity. Due to the large proportion of water in the skin, we assumed a mass density of 1.0 g/cm^3 and a Poisson's ratio equal to 0.5 (Zhang et al., 2011).

Fig. 4 presents the Young's modulus of forearm skin measured in the eight previous predefined directions. Fig. 4 is similar to Fig. 3, it is a kind of dilatation of Fig. 3. So, as for the speed of wave propagation, no significant difference of the Young's modulus can be observed between the different directions, which is confirmed by the Anova statistical analyse. The average values of the skin Young's modulus approximately vary between 22 kPa and 38 kPa as a function of the observation directions. These values are in close agreement with the values observed in the literature, in the same body zone, specially the ones obtained with indentation devices (Jachowicz et al., 2007) (Dikstein and Hartzshark, 1981), which is a similar method to our contactless bio-rheometer that it does not prestress the skin before testing. The theoretical model used (Eq. (2)), seems to be justified, at least for the group G1, and allows a good approximation of the skin Young's modulus. Even though the average values of the skin Young's modulus measured are between 22 kPa and 38 kPa as a function of angular orientation, it could be assumed, in first approximation, that these values are very close and the mechanical behaviour of skin might be assumed as quasi-isotropic for the group G1. The slight differences observed between the skin Young's modulus values versus observation directions might be attributed to the skin structure, more precisely to the density of the skin fibres, collagen or elastic fibres, as a function of their angular orientation. This assumption will be discussed in the next section.

Analysis of the skin microrelief have already been widely used to study evolution of Langer's lines with ageing. The skin relief is composed of lines with variable depths and cutaneous plateau with different geometries (square, rectangle, trapezoid, triangle ...). Hashimoto (1974) (Hashimoto, 1974) proposed to classify the cutaneous lines in two groups: primary lines and secondary lines. The primary lines are clearly marked and their depth range from $30 \mu\text{m}$ to $100 \mu\text{m}$ relative to the skin surface. The primary lines intersect with each other to form the skin plateau. The secondary lines are narrow (depth $5\text{--}40 \mu\text{m}$) and they are located on the cutaneous plateau.

Fig. 5 presents the lines density for the forearm measured in the predefined directions for the group G1. The eight directions were compared with ANOVA test. Globally, no significant difference of density can be observed between the different directions. Indeed, the statistical analysis provides a p-value of 0.903. Therefore, globally, for the group G1, the lines are quasi isotropically distributed.

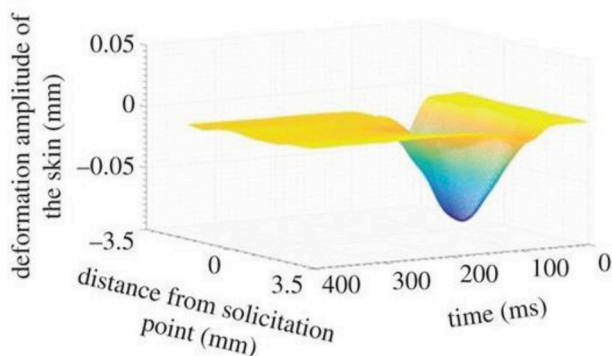


Fig. 2. Skin deformation measured by the linear laser.

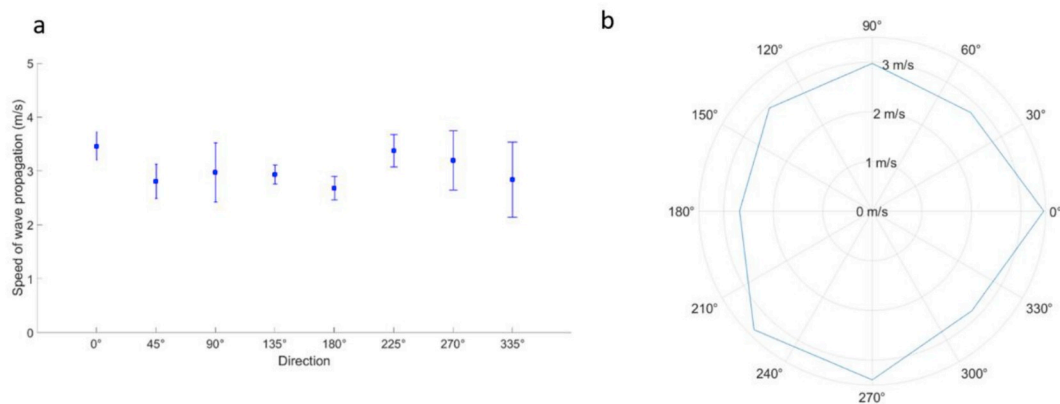


Fig. 3. Speeds of wave propagation for the forearm measured in eight predefined directions for the group G1. The results are presented as (a) mean \pm standard deviation or as (b) polar plot for ease of reading.

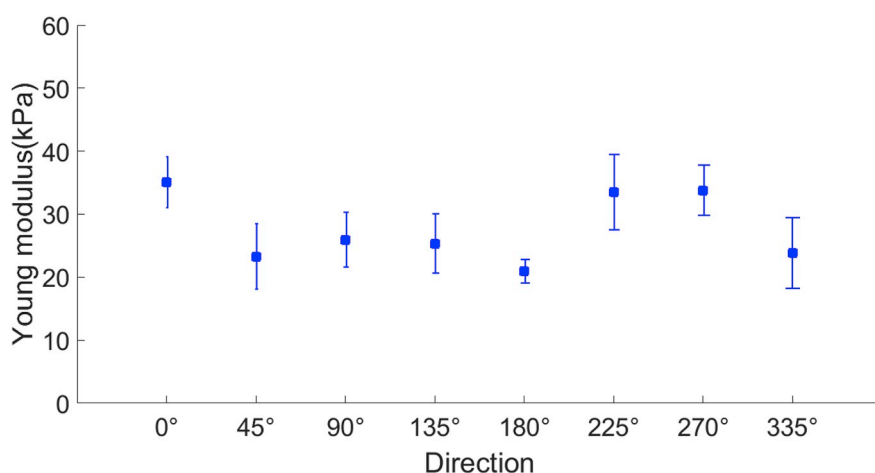


Fig. 4. Young's modulus for the forearm evaluated in eight predefined directions for the group G1. The results are presented as mean \pm standard deviation.

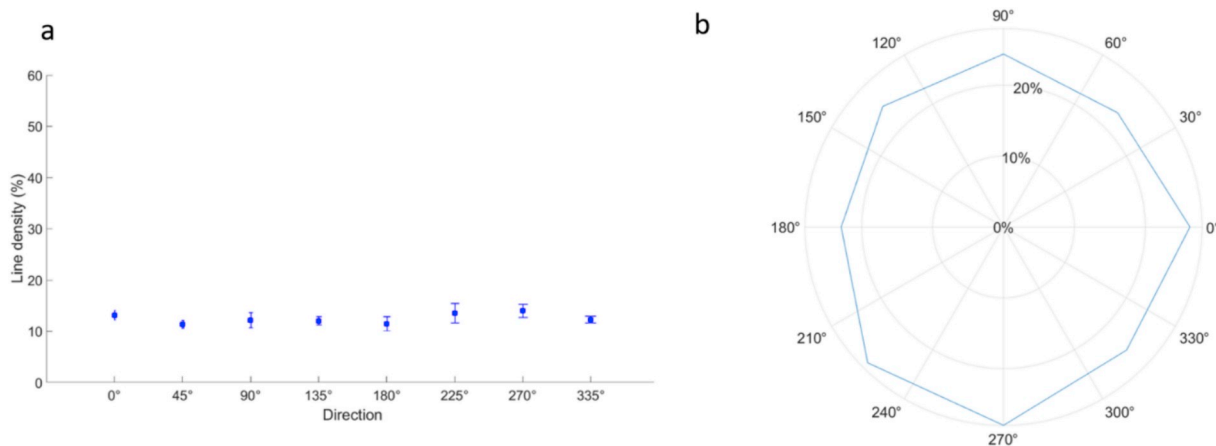


Fig. 5. Density of the cutaneous lines for the forearm evaluated in eight predefined directions for the group G1. These densities have been calculated using watershed transformation from skin 3D-surface image obtained by confocal microscopy. The results are presented as (a) mean \pm standard deviation or as (b) polar plot for ease of reading. No significant difference can be observed (ANOVA analysis: pvalue = 0.903) which seems to indicate that the behaviour is quasi isotropic for the group G1.

In a previous study, skin prints of 116 volunteers were quantified using a Quantimet 720 analyser to assess the cutaneous lines distribution. It has been reported that these lines were relatively isotropically distributed for young people under 20 (Leveque et al., 1984), which is in good agreement with our observation. The evolution of skin surface

relief with ageing has also been studied (Pailler Mattei et al., 2013). For young volunteers (25–34 years old), the authors observed two main directions where the density of the cutaneous lines was a little bit higher than in all the other angular directions. Nevertheless, they showed that cutaneous lines were approximately distributed in all angular directions

onto the forearm for the group of the young volunteers. Our results are then consistent with these conclusions.

Skin morphology constitutes a network of cutaneous lines whose organisation reflects the multi-directional nature of elastic and collagen fibres in the superficial dermis. It has been shown in the literature that Langer's lines followed the direction of preferential orientation of the fibres (Cox, 1941) (Ridge and Wright, 1966). Therefore, our results suggest that for the young skin, the fibres are evenly distributed in the superficial dermis.

The correlation between the speed of wave propagation previously measured and the density of cutaneous lines as a function of the angular orientation, are now analysed. The Spearman statistical analysis was then used for this purpose. The correlation coefficient calculated between the mechanical and the topographical properties of the skin was 0.864 (p -value = $0.0169 < 0.05$), which suggests that there was a significant relationship between them.

Therefore, the skin topography seems to be linked to the bulk mechanical properties of the skin. This phenomenon has already been observed in the literature (Pailler Mattei et al., 2013) (Djaghoul et al., 2018). Zahouani et al. reported that the morphology of the cutaneous lines network reflects the intrinsic tension of the skin (Zahouani et al., 2014). In particular, the authors developed a method to study the chronological ageing of human skin. They showed that the network of lines printed onto the surface of *stratum corneum* reflects the multidirectional tensions of elastic and collagen fibres in the dermis.

2. Effect of ageing on the anisotropy of the skin mechanical and the skin topographical properties

In this part, the effect of ageing on the mechanical and the topographical properties of human skin has been investigated. Fig. 6(a) presents the speed of wave propagation on the forearm measured in the eight predefined directions for the four age groups. Globally, a decrease of the speed wave propagation as a function of ageing process is observed. This decrease is particularly clearly observed from the group G3, so from the volunteers around 40 years old. This observation seems to suggest that the ageing process is not a linear process and it exists a kind of transition age from which the ageing process accelerates. As mentioned previously, the speed of wave propagation on skin is correlated to the skin Young's modulus. Therefore, the results assumed a global decrease of the skin Young's modulus as a function of ageing process in all angular orientations, which has been already observed in the literature (Boyer et al., 2011) (Boyer et al., 2009) (Jachowicz et al., 2007) (Pailler Mattei and Zahouani, 2004). Moreover, the evolution of

the skin Young's modulus versus ageing process seems to progress differently as a function of the different angular direction. Indeed, for the group G1, as previously observed, the skin Young's modulus values are similar whatever the angular direction. With ageing process, the speed of wave propagation on skin values, so the skin Young's modulus, become more important in the direction 225° than for the other directions. For the group G4, which is the older group, two values of the speed of wave propagation on skin were very different than the others: directions 45° and 225° . For these directions, the values of the speed of wave propagation on skin are almost four times higher than for the other directions. Ageing process seems to induce a transition between a quasi-isotropic mechanical behaviour for the young skin and a more underline anisotropic mechanical behaviour for the elderly skin. This transition has always been observed in the literature (Pailler Mattei et al., 2013).

Simultaneously, some changes on the cutaneous lines orientation and the cutaneous lines density as a function of ageing process has been observed (Fig. 6(b)). Indeed, the ageing process induces a strong anisotropy in the cutaneous lines orientation. In particular, the angular distribution of the cutaneous lines indicates that the lines are progressively oriented in two directions about 45° and 225° . These results indicate a strong modification of the cutaneous relief with ageing. In particular, there is a transition from a nearly isotropic distribution of the cutaneous lines in the young skin (G1) to a highly anisotropic distribution in the elderly skin (G4). With ageing, the distribution of the cutaneous lines has already been found to be much more concentrated along the direction at a 45° angle to the axis of arm (Leveque et al., 1984). As for the skin mechanical behaviour, this phenomenon seems to be non linear and occur for the volunteers belonging to the groups G2/G3 and accentuate for the volunteers belonging to the group G4. A transition age on skin topography properties has already been mentioned in the literature for the forearm (Kiguchi and Imada, 2013), which is generally coincide with the decrease of skin's thickness observed between 30 and 40 years of age (Leveque et al., 1984).

This reorientation of the skin lines network is due to a relaxation in the local skin tension with ageing (Pailler-Mattei et al., 2008), which could be confirmed by the previous mechanical observations. Indeed, a Spearman statistical analysis shows a good correlation between the topographical and mechanical properties for each age group (Table 1). As a consequence, the speed of wave propagation on skin is maximal for the directions of maximum lines density. Therefore, skin tension predominates in the Langer's lines direction for all age groups.

The variation of Langer's lines according to ageing process has already been reported in the literature (Cox, 1941). The ageing process

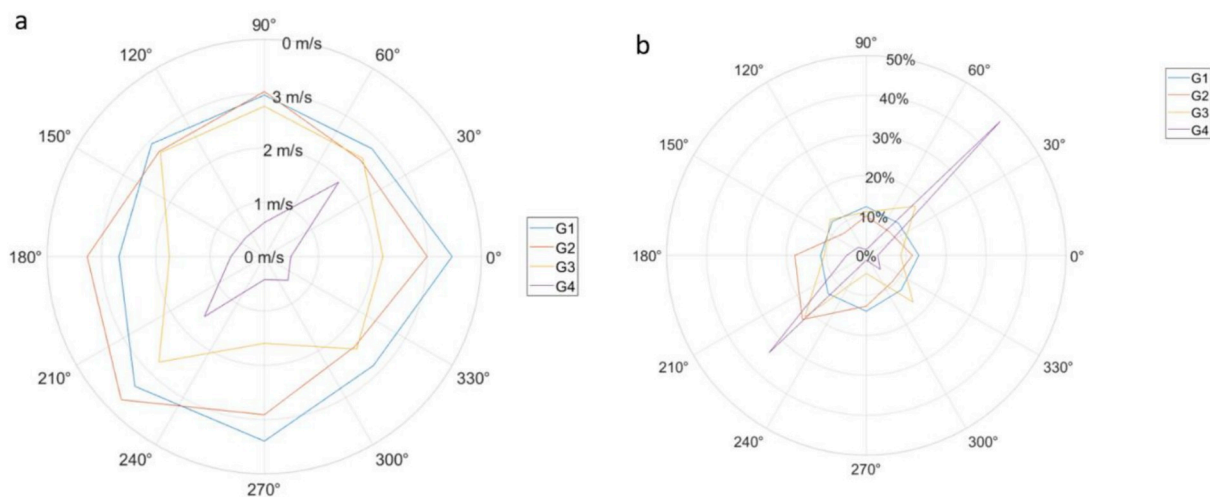


Fig. 6. Ageing effect (from the group G1 to G4) on the anisotropy of (a) speeds of wave propagation (mechanical properties) and (b) density of cutaneous lines (topographical properties).

Table 1

Statistical analysis of correlation between topographical and mechanical properties in the different directions.

	G1	G2	G3	G4
Correlation coefficient	0.86	0.66	0.63	0.97
p-value	0.0169	0.005	0.0083	0.0081

has an important impact on the structure and function of the elastic fibres, which greatly contribute to the skin mechanical response, especially for the elastic response (Baldock et al., 2011). For the young skin, the elastic fibres are highly organised and evenly distributed in the dermis. For the elderly skin, elastin degenerates and aggregates under the dermal-epidermal junction (Suwabe et al., 1999). The global mechanical behaviour of skin is affected by the modification of the elastic fibres system. For aged skin, the elastic fibres do not ensure their elastic response anymore and the Young's modulus of the skin decreases. Furthermore, during ageing process, the distribution of the cutaneous lines becomes much more concentrated along one axis.

As for the skin mechanical properties, a transition between a relative isotropic to a highly anisotropic orientation of the cutaneous lines has been observed as a function of ageing. Both phenomena seem to be related. Therefore, the skin topography might reflect the underlying mechanical condition of the skin.

4. Conclusion

In summary, this study investigated the correlation between topographical and mechanical properties of the skin as a function of ageing. To this end, we presented an innovative contactless bio-rheometer to assess the mechanical behaviour of the skin without contact and in several directions. Concerning the skin lines analysis, we proposed a new method, based on watershed and linear radon transformations, to understand the anisotropy of the skin topography.

Our results showed a good correlation between the skin relief and the mechanical properties of the skin all along the ageing process. With age, we observed a global decrease of the speed of wave propagation, which is related to the Young's modulus. It may be explained by the decrease of collagen and elastic fibres densities. Moreover, there is a transition from an almost isotropic mechanical behaviour to an anisotropic one. In particular, we observed higher tension in the directions 225° and 45°. Concomitantly, the cutaneous lines also undergo modifications. As for the mechanical behaviour, we noticed a transition from isotropic to highly anisotropic orientation of lines. Moreover, it appeared that the speed of wave propagation is maximal for the directions of maximum lines density. Thus, we might conclude that the skin relief reflected the underlying mechanical conditions of the skin.

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