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Research paper

In vivo skin biophysical behaviour and surface topography as a function of ageing

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ABSTRACT

Normal skin ageing is characterised by an alteration of the underlying connective tissue with measurable consequences on global skin biophysical properties. The cutis laxa syndrome, a rare genetic disorder, is considered as an accelerated ageing process since patients appear prematurely aged due to alterations of dermal elastic fibres. In the present study, we compared the topography and the biomechanical parameters of normal aged skin with an 17 year old cutis laxa patient. Skin topography analyses were conducted on normal skin at different ages. The results indicate that the skin relief highly changes as a function of ageing. The cutaneous lines change from a relatively isotropic orientation to a highly anisotropic orientation. This reorganisation of the skin relief during the ageing process might be due to a modification of the skin mechanical properties, and particularly to a modification of the dermis mechanical properties. A specific bio-tribometer, based on the indentationtechnique under light load, has been developed to study the biophysical properties of the human skin *in vivo* through two main parameters: the physico-chemical properties of the skin surface, by measuring the maximum adhesion force between the skin and the bio-tribometer; and the bulk mechanical properties. Our results show that the pull-off force between the skin and the biotribometer as well as the skin Young's modulus decrease with age. In the case of the young cutis laxa patient, the results obtained were similar to those observed for aged individuals. These results are very interesting and encouraging since they would allow the monitoring of the cutis laxa skin in a standardised and non-invasive way to better characterize either the evolution of the disease or the benefit of a treatment.

1. Introduction

The skin surface is not smooth; it has a specific relief which is characteristic of a physiological state and could be modified as a consequence of certain pathologies. The skin relief is composed of lines with variable depths and cutaneous plateau with different geometries (square, rectangle, trapezoid, triangle…).

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It has been proposed to classify the cutaneous lines in two groups: primary lines and secondary lines (Hashimoto, 1974). The primary lines are wide and their depth ranges from 30 μm to 100 μm relative to the skin surface. During ageing process the maximum depth of the primary lines can reach several hundreds of microns to form the wrinkles on the skin. The primary lines intersect with each other to form the skin plateau. The secondary lines are narrow (depth 5–40 μm) and they are located on the cutaneous plateau.

The human skin is composed of three different layers from the inner to the outer: hypodermis, dermis and epidermis. The hypodermis is a loose connective tissue mainly composed of adipocytes and serves as insulation and fat reserve for the body. The dermis consists in a network of collagen with interspersed elastic fibres, blood vessels and lymphatic elements. The collagen fibres act on the resistance of the network while the elastic fibres confer to the network its elasticity (Silver et al., 2001, 2003). All those fibres are immersed in an interstitial fluid composed of proteoglycans, ions and water. This surrounding liquid composition is tightly regulated to provide adequate viscosity, volume and pressure in soft connective tissues (Aukland and Reed, 1993). The outer layer of the skin, the epidermis, acts as a barrier to protect the individual from dehydration and pathogens insults. Epidermis is a living entity consisting in a stratified and cohesive structure resulting from the differentiation of keratinocytes from the basal layer to the stratum corneum (Koster and Roop, 2007).

From a mechanical point of view, the human skin is a living viscoelastic (Manschot and Brakkee, 1986; Pereira et al., 1991; Silver et al., 2001) and a stratified tissue. Many approaches have been developed to study the skin mechanical properties *in vivo* including suction (Khatyr et al., 2006), extension (Lim et al., 2008), torsion (Berardesca et al., 1991), friction (Pailler-Mattei et al., 2011; Zahouani et al., 2009; Sivamani et al., 2003), static and dynamic indentation (Pailler-Mattei et al., 2008; Boyer et al., 2009) and recently a three-dimensional deformations device that allows to measure the skin anisotropic properties (Flynn et al., 2011). The mechanical response of the skin to applied loads involves both a viscous component associated with energy dissipation and an elastic component associated with energy storage (Silver et al., 2002). The viscous behaviour of the human skin can be neglected in first approximation and the skin can then be treated as an elastic material (Bischoff et al., 2000; Delalleau et al., 2006), specially for the young skin and for the light applied loads (Pailler-Mattei et al., 2008).

Because of the increase of life expectancy and of the socio-economic needs to age "healthy", the understanding of the ageing mechanisms becomes an essential issue for society. In this context, the study of the mechanical properties of the human skin *in vivo* and their modifications caused by ageing is a central focus for the cutaneous research (Ryu et al., 2008; Flynn and Mc Cormack, 2010; Krueger et al., 2011).

The natural human skin ageing is conditioned by extrinsic and intrinsic parameters promoting skin elasticity loss and further wrinkles formation due to collagen and elastic fibres progressive degradation; while a change in lipid content of the epidermal barrier is responsible for skin dehydration and thinning (Yaar et al., 2002; Ramos-e-Silva and da Silva Carneiro, 2007). The cumulative exposure to ultraviolet radiations, fatty food intake and cigarette smoking are considered as the major contributors of the extrinsic skin ageing process. Intrinsic skin ageing is mainly related to genetic factors changes overtime such as an imbalance expression of genes contributing to extracellular matrix degradation, and the shortening of chromosomes' telomeres leading to cellular senescence and death. Both extrinsic and intrinsic processes could be relayed by the oxidative stress with dramatic consequences on cell repair machinery and deregulation of long-lived extracellular matrix proteins remodeling (Naylor et al., 2011). One of the most remarkable manifestations of ageing is the loss of tissue elasticity together. The degeneracy of elastic tissues, which are built during development, has consequences for breathing, regulation of pulse pressure, atherosclerosis, aneurysms, hypertension, emphysema, and skin wrinkles (Robert et al., 2008). Dysfunctions of elastic tissue are due to degradation and/or modification of elastic fibres (calcification, lipidation, oxidation or glycation), which are considered as a factors amplifying the inflammation process and the degradation-dependent ageing processes (Fulop et al., 2012). Therefore, elastic tissues can be considered as relevant biomarkers of ageing. Genetic mutations in major components of elastic fibres cause severe diseases of which the cutis laxa syndrome is a heterogeneous group of disorders characterised by a loose, redundant and wrinkled skin giving the patients a prematurely aged appearance (Kielty, 2006). We have thus considered the congenital cutis laxa syndrome as an interesting human model of accelerated ageing of skin since it has never been compared to normal ageing from a biophysical point of view.

This paper aims to compare *in vivo* mechanical measurements and topographical observations from normal skin ageing and skin from a cutis laxa patient. Firstly, indentation tests under light load were realised to observe the variation of the bulk mechanical properties of the skin (Pailler-Mattei and Zahouani, 2006) and the skin physico-chemical surface properties. Secondly, skin relief was assessed by a topographical analysis of skin replicates by interferometry. Finally, we compared the results obtained with healthy individuals at different ages and a cutis laxa patient.

2. Material and methods

2.1. *Determination of the skin tested area*

Topographical analysis and mechanical tests were realised on the same skin area for each volunteer. The surface skin area analysed is always selected in the same way. The method to select the tested area consists in measuring the length of the right inner forearm, noted *L*. From the elbow, a surface of 2 cm × 2 cm located at the quarter of the length *L* is determined and considered as the tested surface.

2.2. *Volunteers panel*

Topographical investigations and indentation tests were realised on eighteen volunteers Caucasian women: sixteen healthy volunteers aged from 25 to 75 years old, one 17 years