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ORIGINAL ARTICLE

Effects of skin wrinkles, age and wetness on mechanical loads in the stratum corneum as related to skin lesions

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Abstract Finite element models of skin were developed to determine the effects of wetness, age, and wrinkles on mechanical strains and stresses in the stratum corneum (SC) as related to skin lesions. We modeled two geometries, young (0.12-mm-deep wrinkles) and aged (0.18-mm-deep wrinkles), and for each geometry, three loading conditions were applied (compression in a dry environment, compression and shear in dryness, and compression with shear in wetness). Effects of skin wrinkling were studied independently or while coupled with age-related mechanical property changes. For each simulation, we calculated the peak maximal shear strain and stress in the SC, peak shear stress on the skin surface, and volumetric exposure of the SC to potentially injurious shear stresses (<70 kPa). Compression and shear with wetness produced the highest skin surface loads. Volumetric exposure of aged skin to potentially injurious shear stresses was six times greater than in the young skin for these conditions. Deeper wrinkles caused elevated loads in the SC consistently for all outcome measures and independently of the age factor. Thinning and/or stiffening the SC increased both the surface and internal SC stresses. Our findings indicate that theoretically, wetness, skin aging, and/or skin wrinkling are all risk factors for skin lesions such as superficial pressure ulcers.

Keywords Finite element model · Coefficient of friction · Wrinkles · Aging · Shear stress

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1 Introduction

Skin lesions are one of the most common injuries in elderly, paralyzed, and immobilized patients. Pressure ulcers (PUs) involving skin damage are one particular type of a skin lesion, which, if not treated timely, may result in severe complications such as infections, sepsis, and osteomyelitis [1]. Such superficial pressure ulcers (SPUs) are predominantly caused by frictional forces and shear stresses, and their development is a direct result of skin breakdown [14].

Several factors have been proposed in the biomedical literature as being associated with an increased risk of developing skin lesions at large, and SPUs in particular. Prolonged pressures, frictional forces, and shear stresses, as well as the combination of these, have been characterized as decisive mechanical factors in the development of skin lesions. Such skin lesions include not only SPUs but also macerations, excoriations, blisters, abrasions, moisture lesions, and skin tears. All these types of skin damage typically develop in elderly patients and in patients confined to wheelchairs and beds [10, 11, 24]. Frictional forces may contribute to the formation of skin lesions by stripping the stratum corneum (SC) and therefore making the skin more susceptible to infections. A combination of pressures and shear stresses, which is always present in real-world conditions, may cause the dermal blood vessels to be distorted and angulated in a manner that impairs blood perfusion and therefore hampers metabolism [7, 24]. Using a pig model, it has been previously shown that skin breakdown associated with formation of skin lesions occurs when applying shear stresses higher than approximately 70 kPa on the skin surface [13].

Furthermore, wetness or moisture between the skin and textiles, caused due to perspiration, bowel or bladder incontinence or drainage from fistulas or wounds, is known to increase the coefficient of friction (COF) between the skin and the contacting textile. These factors may consequently increase frictional forces and shear stresses on and within the skin [10, 11, 24]. It has been further claimed that wetness or moisture on the skin surface render the skin limp and less resistant to friction, thereby increasing the risk of its breakdown [1, 7, 24]. Wetness and moisture are therefore critical risk factors for skin lesions.

In addition, factors such as age [5, 7], anatomical site [18], individual orientation of Langer lines [5, 18], dryness of the skin [12], and systemic pathologies, particularly diabetes [7], are known to influence the skin structure, topography, and mechanical properties, and for this reason may be associated with the development of skin lesions, including SPUs. Wrinkling is one characteristic of the aged skin, and has been attributed to age-dependent loss of tissue hydration and to changes in the density and orientation of collagen fibers and keratin in the extracellular matrix [5]. An inherent limitation of patient studies in this field is, however, that it is difficult and sometimes impossible to isolate the contribution of potential individual risk factors, such as wrinkling, to skin lesions, and therefore, patient studies need to be accompanied by theoretical modeling, which allows insights into mechanisms. The effects of skin wrinkling, in particular, on the risk for skin lesions have not been previously studied, neither experimentally nor theoretically.

Finite element (FE) computational models are increasingly being used for studying the etiology of PUs [16], and in particular, to identify risk factors for PUs [9]. In skin research, FE models have also been used for studying fold and wrinkle formation in young and aged skins, mostly in the context of cosmetics [4–6, 18]; nevertheless, FE was never used to study wrinkling as a risk factor for skin lesions. The aim of this study was therefore to develop FE models of the skin in order to examine effects of wetness, age, and skin wrinkles on concentrated mechanical loads (strains/stresses) in the skin as related to skin damage.

2 Methods

In order to determine effects of wetness, age, and skin wrinkles on strains and stresses in the skin during sitting or lying, we used a set of six models. Specifically, there were two model geometries—one for young and the other for aged skin (Fig. 1), and for each geometry, three loading conditions were applied, simulating pure compression in a dry environment, compression combined with shear in a dry environment, and compression combined with shear in a wet environment.

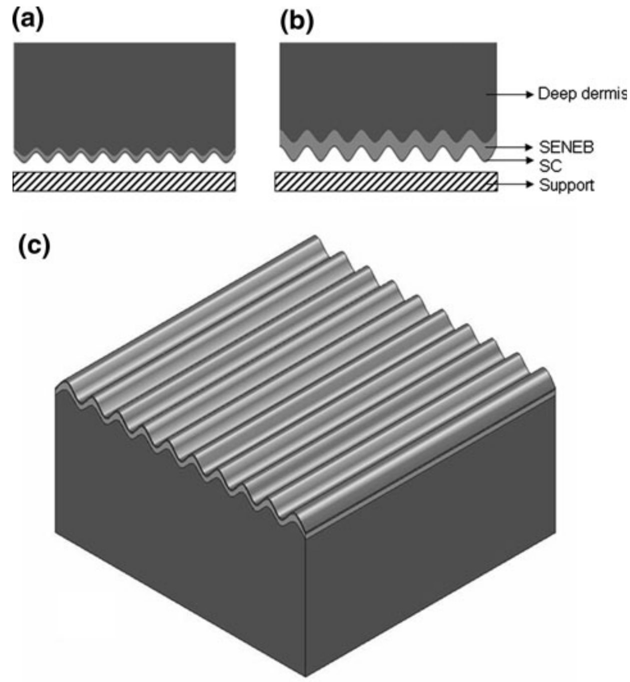

Fig. 1 Finite element model geometries simulating an approximately 3 mm × 3 mm × 1.3 mm-sized young (**a**) and aged (**b**) skin samples. Isometric view of the young skin (**c**) is brought for illustration of the three-dimensional features. Both geometrical model configurations consist of three layers: stratum corneum (*SC*), epidermis plus upper dermis (subepidermal nonechogenic band, *SENEB*), and deep dermis

Two geometrical model configurations were built to represent young and aged skin anatomies and topographies using the SolidWorks 2008 solid modeling software (ver. SP2.1, Dassault Systèmes SolidWorks Corp., MA, USA). These models simulated three-dimensional (3D) skin samples with approximate size of 3 × 3×1.3 mm (length × width × height), and each model consisted of three layers, representing the SC, the epidermis plus upper dermis (subepidermal nonechogenic band, SENEB), and the deep dermis (Fig. 1). The topographies of the young and aged skins and the thicknesses of the three skin layers in each age model were adopted from the literature [2, 15, 18], and are specified in Tables 1 and 2, respectively.

The three skin layers were assumed to be nonlinear elastic and isotropic materials. Their large deformation

Table 1 Topographical specifications of the sets of the young and aged skin-simulating models

	Young skin	Aged skin	Reference
Skin wrinkle width (mm)	0.26	0.33	[2]
Difference between peaks and troughs in a wrinkle (mm)	0.12	0.18	[15]

Table 2 Geometrical specifications, mechanical properties, and numerical characteristics of the sets of the young and aged skin-simulating models

Layer	Young skin				Aged skin			
	Thickness (mm)[a]	Shear modulus (MPa)[b]	Bulk modulus (MPa)	Number of mesh elements[c]	Thickness (mm)[a]	Shear modulus (MPa)[b]	Bulk modulus (MPa)	Number of mesh elements[c]
SC	0.015	2	199	66,231	0.015	4[d]	399	115,727
SENEB	0.05	0.02	2	65,527	0.2	0.02	2	293,487
Deep dermis	1.235	0.2	19.9	155,346	1.085	0.33	33	195,335

SC stratum corneum, *SENEB* subepidermal nonechogenic band

[a] Data were adopted from the literature [18]. Thickness of the whole skin was 1.3 mm in both the young and the aged skin models

[b] Data were adopted from the literature [18]. Poisson's ratios were taken as 0.495 for all skin layers in all models

[c] The support mesh included 2,579 and 3,452 elements in the young and the aged skin-simulations, respectively. All elements were 4-node linear tetrahedron (type C3D4 in ABAQUS)

[d] For dehydrated SC

behavior was described using a neo-Hookean material model, with strain energy density function W:

$$W = \frac{G}{2}\left(\lambda_1^2 + \lambda_2^2 + \lambda_3^2 - 3\right) + \frac{k}{2}(J-1)^2, \quad (1)$$

where G is the shear modulus, k is the bulk modulus, λ_i are the principal stretch ratios, and $J = det(F)$, where F is the deformation gradient tensor. Constitutive constants G for each skin layer were adopted from previous studies [18] and are provided in Table 2; bulk moduli were calculated for each skin layer under the assumption that Poisson's ratios of each layer were 0.495 (Table 2).

In order to test the effect of compressive loading on skin, the skin was simulated to be compressed against a soft support with mechanical properties that are characteristic to hospital mattresses or wheelchair cushions: elastic modulus of 70 kPa and Poisson's ratio of 0.4 [17]. The skin was compressed against the support until reaching a mean interface pressure of approximately 7 kPa, which is typical for average contact pressures under the buttocks during sitting, recumbency, or horizontal lying [8, 10]. To test the effect of shear in combination with compression, we further imposed a boundary condition of a horizontal 0.1-mm displacement between the skin and the support.

Two different COF were defined between the skin surface and the support, based on experimental studies, where skin samples were rubbed against commercially available hospital fabrics [10, 11]. These COF were 0.42 for dry contact and 0.92 for wet contact [11]. "Fixed" interfaces ("no-slip" condition) were assumed between all skin layers, and transitions between them were modeled as discontinuous.

Hence, in total, six models were produced, representing two geometries (young and aged skins), and simulating three loading cases for each: pure compression in a dry environment, combined compression and shear in a dry environment, and combined compression and shear in a wet environment. We used the ABAQUS FE solver (ver. 6.8-2, SIMULIA, RI, USA) in its non-linear large-deformation analysis mode. Automatic meshing was used, and meshes included approximately 290,000 and 600,000 4-node linear tetrahedron elements (type C3D4 in ABAQUS) in total, in the young and the aged skin geometries, respectively (Table 2). To ensure successful meshing, finer meshes were used in the SC and SENEB layers with respect to the deep dermis layer (Table 2). Each simulation took between 4 and 5 h to run on a Pentium processor-based workstation.

For each model, we calculated distributions of maximal shear strains and stresses internally in the SC as well as distributions of surface shear stresses and contact pressures on the skin at the skin-support interface. We identified peak values of each of the aforementioned loading measures. We further determined volumetric exposures of the SC to an above-critical shear stress level of 70 kPa [13] by calculating the ratio of volume of elements bearing maximal shear stress above 70 kPa over the volume of the entire SC layer. For each outcome measure, we calculated the ratio of corresponding values for the aged over the young skin to identify trends of effects of the age factor.

Furthermore, in order to isolate the effect of wrinkling on the above outcome measures, i.e. to determine whether skin wrinkling—independently of age—is a risk factor for skin damage, two additional model variants were produced: (1) a model with "aged" skin topography and geometry (Tables 1, 2) that was assigned "young" mechanical properties (Table 2) and (2) a model with "young" skin topography and geometry (Tables 1, 2) that was assigned "aged" mechanical properties (Table 2). Each of these two later model configurations was used to simulate the three aforementioned loading conditions. Ratios of corresponding outcome measures for aged skin geometry over young skin geometry models, while assigning the same mechanical properties—either "young" or "aged"—to both geometrical models, were further calculated. These ratios hence reveal the effect of a change in skin wrinkling in isolation from the effect of changes in skin mechanical properties.

Finally, sensitivity analyses were conducted to evaluate effects of mild variations (±30%) in values of the skin-support COF, as well as the shear modulus of the SC and its thickness (e.g. due to biological variability) on the aforementioned outcome measures. For the purpose of these sensitivity analyses, we changed one input parameter value at a time, keeping all other parameters at their nominal values which were specified above.

3 Results

Changes in the width of wrinkles in the deformed models with respect to the undeformed configurations were all found to be negligible, below 1%. Example distributions of maximal shear strains and stresses in one of the skin models (simulating combined compression and shear loading of young skin in a wet environment) are shown in Fig. 2a, b, respectively. Shear strains were found to peak at the SENEB layer, under the wrinkle troughs. Shear stresses, on the contrary, were found to peak in the SC, specifically at the wrinkle peaks. Example distributions of surface shear stresses and contact pressures on the surface of the same skin model are shown in Fig. 3a, b, respectively. Surface shear stresses and contact pressures were also found to reach their maximal values at the wrinkle peaks.

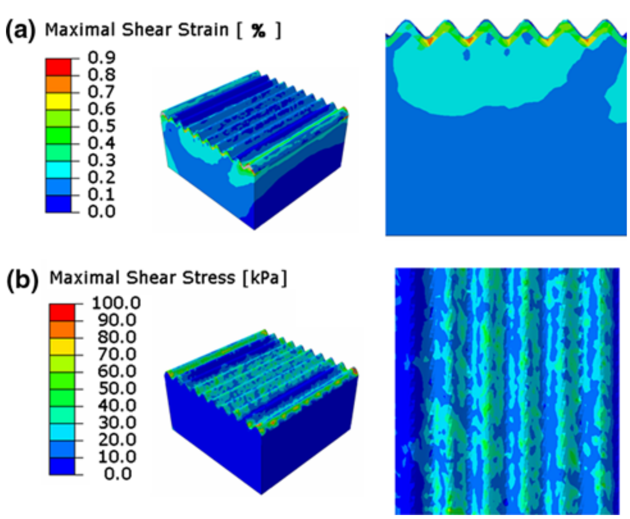

Fig. 2 Example distributions of mechanical loads in the young skin in the model simulating a combination of compression and shear loading in a wet environment: **a** maximal shear strains (*left panel* isometric view, *right panel* side view); **b** maximal shear stresses (*left panel* isometric view, *right panel* superior view)

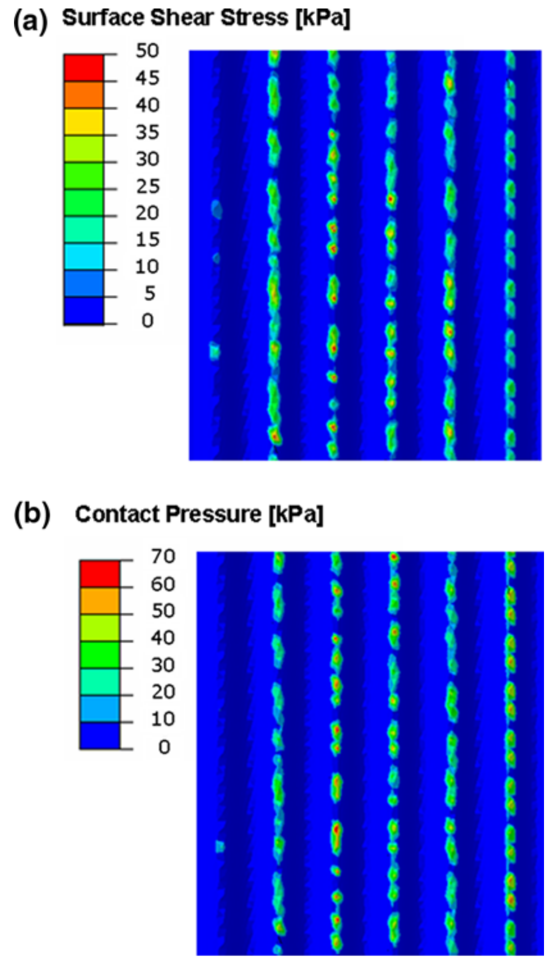

Fig. 3 Example distributions of **a** shear stresses and **b** contact pressures on the skin surface in the model simulating combined compression and shear loading of young skin in a wet environment. Both distributions are shown from a superior view

Data of peak maximal shear strains and stresses in the SC and peak shear stresses on the skin surface, for each of the six models, are shown in Fig. 4. It is evident that in both the young and the aged skin simulation sets, the combination of compression and shear in a wet environment produced the highest values of peak loads on the skin surface and internally in the SC (Fig. 4). In addition, one can clearly see that in the aged skin simulations, peak values of maximal shear stresses internally in the SC and on the skin surface are consistently higher compared to the corresponding values in the young skin simulations (Fig. 4b, c). Strains were similar, however, between the young and aged skins, with slightly higher values for the young skin (Fig. 4a).

Volumetric exposures of the SC to above-critical shear stresses are shown in Fig. 5. Consistently with the trend observed for peak shear stress values, it is evident, in both

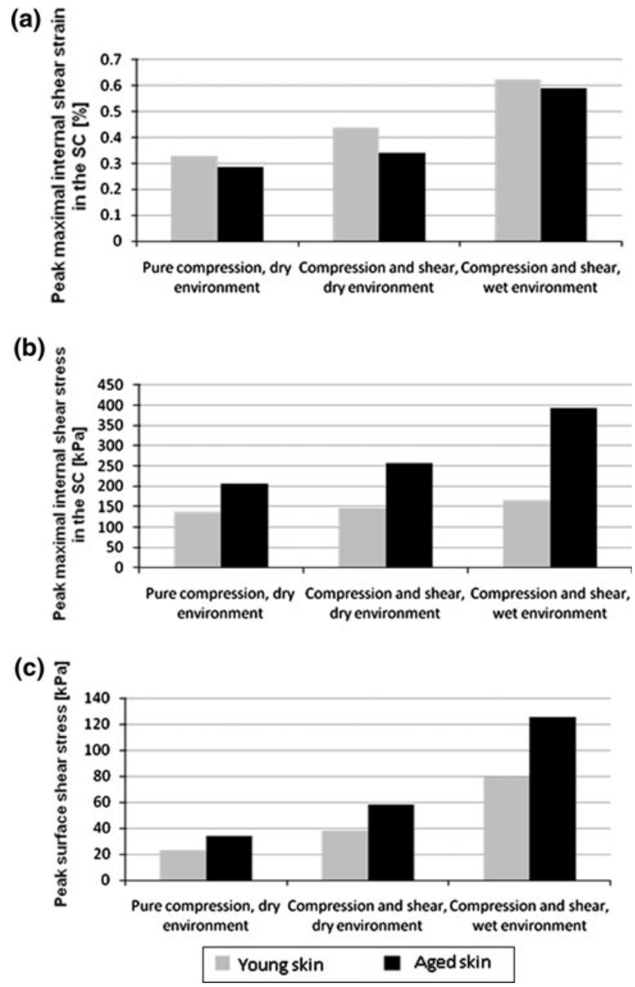

Fig. 4 Peak maximal internal shear strains (**a**) and stresses (**b**) in the stratum corneum (*SC*) and surface shear stresses on the skin (**c**), calculated for the young and aged skin model configurations in the three loading cases (*horizontal axis labels*)

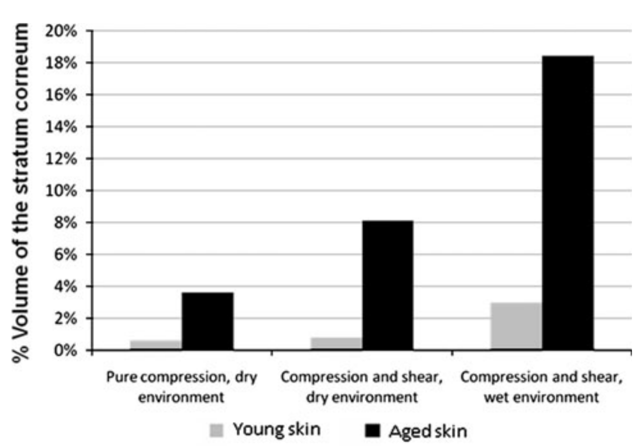

Fig. 5 Percentage of stratum corneum volume that exceeds a critical shear stress level of 70 kPa, calculated for the young and aged skin model configurations in the three loading cases (*horizontal axis labels*)

the young and aged skin simulation sets, that the volumetric exposure to potentially injurious shear stresses (70 kPa, [13]) is increased in the models simulating combined compression and shear in a dry environment compared to a pure compression loading (Fig. 5). The highest volumetric exposure values were again observed in the models simulating loading conditions of combined compression and shear in a wet environment (Fig. 5). When comparing the volumetric exposures between the aged and young skins, it is evident that the exposure of aged SC to potentially injurious shear stresses [13] is considerably higher, being about six times greater than in the young skin for combined compression-shear loading in a wet environment, as shown in Table 3 which specifies aged over young property ratios.

Ratios of corresponding outcome measures for aged skin geometry over young skin geometry models, while assigning the same mechanical properties—either "young" or "aged"—to both geometrical models, are provided in Table 4. All ratios exceeded unity, thereby demonstrating that deeper wrinkles caused elevated mechanical loads in the SC, consistently for all outcome measures (Table 4). The volumetric exposure of the SC to above-critical shear stresses was found to be the outcome measure that was affected to the greatest extent by the increased wrinkle depth as evident by the aged over young skin data presented in Table 4.

The results of the sensitivity analyses for the young and aged skin models and for the different loading conditions are provided in Table 5. Sensitivity of the outcome measures was shown to be the greatest for variations in thickness of the SC and lower for variations in its shear modulus (G) and the skin-support COF (Table 5). Specifically, an increase in the SC thickness resulted in a consistent trend of decrease in all strain and stress measures, whereas a decrease in its thickness had the opposite effect. Volumetric exposures of the SC to above-critical stresses [13] in the young skin showed the highest sensitivity to ±30% changes in SC thickness; however, this high sensitivity was apparently because the absolute volumetric exposures in the young skin were relatively low, below 3% (Fig. 5). An increase in G of the SC consistently caused a decrease in peak maximal shear strains internally in the SC as well as an increase in all stress measures, whereas a decrease in G generally caused the opposite (excluding three shear stress calculations in simulations of pure compression in a dry environment; Table 5). For the ±30% changes in G, peak maximal shear strains internally in the SC and its volumetric exposures to above-critical shear stresses were the most affected outcome measures (Table 5). An increase in the skin-support COF generally caused an increase in all outcome measures, whereas a decrease in the COF overall caused the opposite trend, with

Table 3 Ratios of corresponding aged skin over young skin outcome measures for the three loading cases considered herein

Ratios of "aged" over "young" skin outcome measures	Loading case		
	Pure compression, dry environment	Compression and shear, dry environment	Compression and shear, wet environment
Peak maximal shear strain internally in the SC	0.88	0.78	0.95
Peak maximal shear stress internally in the SC	1.50	1.77	2.37
Peak shear stress on the skin surface	1.48	1.51	1.57
Volumetric exposure of the SC to above-critical shear stress[a]	5.93	9.97	6.19

SC stratum corneum

[a] The critical shear stress value, of 70 kPa, was adopted from the literature, based on experiments, where shear stresses were applied on the skin of a porcine animal model [13]

Table 4 Ratios of corresponding outcome measures for aged skin geometry over young skin geometry models, while assigning the same mechanical properties—either "young" or "aged"—to both geometrical models

	Loading case		
	Pure compression, dry environment	Compression and shear, dry environment	Compression and shear, wet environment
"Young" mechanical properties			
Peak maximal shear strain internally in the SC	1.58	1.35	1.65
Peak maximal shear stress internally in the SC	1.62	1.39	1.92
Peak shear stress on the skin surface	1.76	1.35	1.42
Volumetric exposure of the SC to above-critical shear stress[a]	4.98	5.43	4.67
"Aged" mechanical properties			
Peak maximal shear strain internally in the SC	1.36	1.36	1.30
Peak maximal shear stress internally in the SC	1.03	1.31	1.58
Peak shear stress on the skin surface	1.10	1.55	1.38
Volumetric exposure of the SC to above-critical shear stress[a]	1.96	2.87	1.97

SC stratum corneum

[a] The critical shear stress value, of 70 kPa, was adopted from the literature, based on experiments, where shear stresses were applied on the skin of a porcine animal model [13]

several exclusions (the peak maximal shear strain internally in a wet SC of a young skin subjected to compression and shear decreased when the COF increased, and there were three other exceptions with negligible extents; Table 5). The peak shear stress on the skin surface was the outcome measure that was influenced to the greatest extent by COF changes (Table 5). Additionally, wetness generally amplified the effect of COF changes on shear strains and stresses (Table 5). Finally, the sensitivity analyses showed that variations in the input parameters overall affected the outcome measures in the young and aged skins to similar extents (Table 5).

4 Discussion

In this study, we tested the effects of skin wrinkles, age, and wetness on mechanical loads in the SC. The former two factors are not completely independent as a general relationship is well known between age and wrinkling (although some individuals experience more wrinkles at a younger age). We successfully developed biomechanical FE models of skin which simulated wrinkling, aging, and wetness, and examined the effects of these factors on concentrated strains and stresses in skin, particularly in the SC which is the first barrier against infections (and hence its loading is critical in the context of skin lesions). The results show that shear stresses in the SC are elevated when the skin ages, when the skin has deeper wrinkles (either independently of age or due to aging), and also when the skin is exposed to a wet environment (Figs. 4, 5). The present findings thus support previous medical research and clinical experience which suggested wetness as a risk factor for SPU formation, especially among elderly patients [10, 11, 24]. Based on the present theoretical modeling, wetness of the skin in weight-bearing body regions of

Table 5 Sensitivity analysis of effects of mild variations in the input parameters on model predictions

Model input parameters	Thickness of SC		Shear modulus of SC		Skin-support COF	
Variation	+30%	−30%	+30%	−30%	+30%	−30%
Effects on model predictions						
Young skin						
Peak maximal shear strain internally in the SC						
Pure compression, dry environment	−13.49	12.71	−14.98	24.10	3.39	−4.11
Compression and shear, dry environment	−11.76	2.78	−14.84	24.34	14.19	−4.86
Compression and shear, wet environment	−3.86	9.68	−16.03	24.31	−6.20	−29.33
Peak maximal shear stress internally in the SC						
Pure compression, dry environment	−31.45	65.02	17.62	4.49	0.09	0.07
Compression and shear, dry environment	−20.75	54.10	9.34	−2.56	0.35	1.44
Compression and shear, wet environment	−15.34	39.14	8.32	−2.10	9.50	−8.62
Peak shear stress on the skin surface						
Pure compression, dry environment	−13.58	112.38	18.86	13.32	27.67	−29.00
Compression and shear, dry environment	−24.47	30.88	0.23	−0.59	31.37	−31.15
Compression and shear, wet environment	−23.49	38.88	1.37	−0.52	12.67	−36.93
Volumetric exposure of the SC to above-critical shear stress[a]						
Pure compression, dry environment	−88.96	249.22	25.34	−42.26	0.69	−6.01
Compression and shear, dry environment	−80.54	381.12	28.25	−36.92	52.50	−14.19
Compression and shear, wet environment	−73.42	277.65	22.71	−34.37	32.29	−62.52
Aged skin						
Peak maximal shear strain internally in the SC						
Pure compression, dry environment	−5.45	73.25	−16.11	26.91	−0.82	−2.80
Compression and shear, dry environment	−16.04	47.38	−18.61	31.32	14.38	−5.13
Compression and shear, wet environment	−23.46	25.12	−18.64	30.79	42.73	−33.13
Peak maximal shear stress internally in the SC						
Pure compression, dry environment	−15.59	102.95	9.09	−4.18	4.20	−0.50
Compression and shear, dry environment	−23.92	68.73	7.09	−11.49	13.35	−9.88
Compression and shear, wet environment	−27.32	35.29	6.60	−11.23	40.26	−22.47
Peak shear stress on the skin surface						
Pure compression, dry environment	0.07	82.65	1.62	37.45	82.40	−18.14
Compression and shear, dry environment	−31.20	57.47	3.79	−5.85	29.56	−30.06
Compression and shear, wet environment	−26.33	72.20	4.15	−6.32	36.98	−33.26
Volumetric exposure of the SC to above-critical shear stress[a]						
Pure compression, dry environment	−64.13	146.10	12.16	−28.01	0.42	−2.47
Compression and shear, dry environment	−69.52	38.30	12.72	−24.94	27.46	−18.46
Compression and shear, wet environment	−54.14	59.95	7.93	−14.07	63.94	−40.79

Effects on outcome measures are reported as % change with respect to the values obtained for the nominal input parameter set

COF coefficient of friction, *SC* stratum corneum

[a] The critical shear stress value, of 70 kPa, was adopted from the literature, based on experiments, where shear stresses were applied on the skin of a porcine animal model [13]

individuals confined to wheelchairs or beds should be avoided to the extent possible. On the other hand, our simulations imply that oil-based creams or lotions, as well as dressing materials with a COF-reduction effect such as those discussed in previous studies [22, 23], are advantageous as our data showed that low COF decreased the exposure of the SC to potentially injurious shear stress levels (Fig. 5, right bars; Table 5). These findings particularly correspond with previous clinical studies which have shown that dressings designed to reduce shear forces through a COF-reduction mechanism may be effective for preventing skin erythema, which indicates early skin damage [3, 20, 21]. Our sensitivity analyses further revealed that the skin micro-anatomy and mechanical properties are also important factors influencing the susceptibility to skin damage. Specifically, the sensitivity analyses demonstrated that a thin and/or stiff SC tends to develop high surface and internal stresses (Table 5), and hence, thin/stiff SC can be recognized as risk factors for skin lesions. In the dermatological literature, a condition called "skin atrophy", which is thin, wrinkled skin, is often being associated with skin fragility. Indeed, a recent study which examined the susceptibility of patients with cancer to PUs identified deepening of skin wrinkles (independently of age) as a risk factor for SPUs [19], which provides additional clinical support to the present findings.

Some limitations of the modeling should be taken into account when interpreting the findings. First, we did not directly validate the present results, but evidence from clinical trials support our findings regarding the contribution of skin wrinkles to the risk for skin damage [19], as well as regarding the importance of reducing the COF at the skin-support interface [3, 20, 21]. Second, in this study, the skin was modeled as a three-layered structure, based on a biomechanical model formulated by Magnenat-Thalmann et al. [18], which, to the best of our knowledge, is one of the most detailed skin models available in the literature in terms of description of layer thicknesses and mechanical properties of the individual layers. However, we could not find detailed topographical representations of young and aged skins in a single report, and therefore, topographical parameters were adopted from two other studies [2, 15]. Third, the hypodermis was not taken into account; the skin layers were all assumed to be isotropic, and the skin wrinkles were assumed to extend infinitely and to have identical shapes per each geometrical configuration, which obviously lacks a representation of the full complexity of the skin microarchitecture. In future studies, it is particularly worthwhile to investigate the inhomogeneity of wrinkle structures, perhaps with anisotropic mechanical properties of the layers, and their potential effects on mechanical loads in skin. The present approach, however, allowed quantification of shear strain/stress differences between models representing young and aged skins and subjected to different loading conditions, without needing a large number of geometrical configurations. A fourth limitation in the modeling was that the imposed boundary conditions corresponded to simplified loading conditions, simulating two loading variations: pure compression or combined compression and shear of a skin sample against a support. Nevertheless, this simplification again allowed us to test a relatively large number of different model variants (18 "young" and 18 "aged" skin simulations) in the framework of the sensitivity analyses. Considering the above-discussed and other potential limitations, we recommend that our present strain/stress data be interpreted mostly as trends of effects, rather than as absolute values.

In conclusion, this is the first study in which a FE approach has been used to evaluate whether skin wrinkling, aging, and wetness are risk factors for skin lesions, and our findings strongly indicate that theoretically, they all are. Future work will include full-3D non-linear large-deformation FE modeling simulating compression, tension and shear of skin samples with inhomogeneous wrinkle shapes and anisotropic layer properties, against supports with different mechanical properties. The direct effect of moisture on the mechanical properties of skin is also planned to be taken into consideration.

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