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Infant Skin Microstructure Assessed In Vivo Differs from Adult Skin in Organization and at the Cellular Level

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Abstract: **Functional differences between infant and adult skin may be attributed to putative differences in skin microstructure. The purpose of this study was to examine infant skin microstructure in vivo and to compare it with that of adult skin. The lower thigh area of 20 healthy mothers (ages 25–43) and their biological children (ages 3–24 months) was examined using in vivo noninvasive methods including fluorescence spectroscopy, video microscopy, and confocal laser scanning microscopy. Stratum corneum and suprapapillary epidermal thickness as well as cell size in the granular layer were assessed from the confocal images. Adhesive tapes were used to remove corneocytes from the outer-most layer of stratum corneum and their size was computed using image analysis. Surface features showed differences in glyph density and surface area. Infant stratum corneum was found to be 30% and infant epidermis 20% thinner than in adults. Infant corneocytes were found to be 20% and granular cells 10% smaller than adult corneocytes indicating a more rapid cell turnover in infants. This observation was confirmed by fluorescence spectroscopy. Dermal papillae density and size distribution also differed. Surprisingly, a distinct direct structural relationship between the stratum corneum morphology and the dermal papillae was observed exclusively in infant skin. A change in reflected signal intensity at ~100 μm indicating the transition between papillary and reticular dermis was evident only in adult skin. We demonstrate in vivo qualitative and quantitative differences in morphology between infant and adult skin. These differences in skin microstructure may help explain some of the reported functional differences.**

Healthy infant skin is often described as soft and tender and is frequently presented as an ideal state of skin aspired to by adults. On the other hand, infant skin is also described as "fragile" and "sensitive" and is prone to dermatitides and infections (1). Of particular importance is the recent increase in the incidence of infantile atopic dermatitis (2). A compa-

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rative study of infant and adult skin physiology is bound to shed light on the reasons for this special status of infant skin.

The barrier function and the water holding and transport properties of infant stratum corneum (SC) have been shown to be different from an adult and continue to evolve through the first year of life (3). Infant SC was found to have higher water content and higher transepidermal water loss rates at rest, absorb more water and loose excess water faster than adult SC. Many of these differences may be explained by careful examination of the underlying skin microstructure.

Advances in noninvasive methods such as confocal laser scanning microscopy (CLSM) have made the study of skin microstructure in vivo possible, avoiding the need for painful biopsies, as well as the artifacts introduced by handling and fixing the sample required for histological samples examination. By focusing the incident light on the skin at different depths and scanning its position in the plane parallel to the skin surface, one can obtain images corresponding to "optical sections" through the skin volume, in contrast to the vertical sections of histology (4). This technology has been applied to the study of adult skin physiology (5) and pathology of several dermatological conditions [for reviews see (4,6,7)], but to our knowledge it has not yet been used in the study of infant skin.

Another useful noninvasive method is in vivo fluorescence spectroscopy, which has been used to assess the proliferation rate of the epidermal cells (8–10). This signal has been shown to decrease with age in adults (11), but there have been no reports to date about its use on infant skin. In this study, we employed in vivo noninvasive methods to address the question whether infant skin microstructure is different from that of an adult at the organ level (epidermal thickness, epidermal organization) and at the cellular level (cell size and cell density).

MATERIALS AND METHODS

Clinical Protocol

The study was performed under approval from an independent institutional review board and following the principles of the Declaration of Helsinki. Twenty mothers from the New Jersey area at 25–46 years of age and their biological infants at ages 6–24 months participated in the study. Adult subjects signed a written informed consent for themselves and their participating children. Only healthy individuals were recruited. The skin phototypes of the adult subjects were I–III on the Fitzpatrick scale. The infant population was fair complexioned and equally distributed between boys and girls. Subjects were instructed to avoid use of skin care products on the arms and legs for at least 24 hours before the measurements. Visibly distressed or crying infants were excluded. Measurements were performed on the upper inner arm, the dorsal forearm, or the lower thigh area as described below.

Video Microscopy

A video microscope (HiScope Systems Co., Closter, NJ) was used to acquire in vivo light reflectance images of the skin surface with a magnification of 100×. The microscope camera was calibrated before image acquisition using a white reflectance standard (Minolta, Ramsey, NJ). The final image corresponded to a skin area of 2.7 mm × 2.1 mm.

Confocal Laser Scanning Microscopy

The skin sites of interest were examined in vivo using a reflectance CLSM (Vivascope® 1500, Lucid Inc., Henrietta, NY) equipped with a laser at 785 nm (laser power < 25 mW at the tissue surface) and a oil immersion 30× objective of numerical aperture 0.9 NA. This microscope generates a series of consecutive optical sections every 3.125 μm of increasing depth. Imaging starts at the top layer of the SC and progresses down through the epidermal layers, the dermal epidermal junction, and the top layers of the dermis. Each optical section corresponded to a skin area of 0.5 mm × 0.5 mm. The laser power was adjusted to increase the signal-to-noise ratio for the deeper sections and its value was recorded for each corresponding image. The sequential optical sections were analyzed as explained below for the measurement of SC and epidermal thickness and they were reconstructed to form three-dimensional images using the 3D Constructor® plug-in to Image Pro software (Media Cybernetics, Bethesda, MD). The lower thigh area was selected for theses measurements to reduce infant motion during acquisition. Three replicate stacks within a 4 mm × 4 mm area were sampled and then averaged.

CLSM Image Analysis

The SC thickness was calculated as the number of images from the first image (top corneocyte layer) to the image just before the one where granular cells can be detected, times the imaging step (3.12 μm). Similarly, the epidermal thickness was calculated as the number of images from the top corneocyte layer to the image just before the one where the top of the dermal papilla can be detected, times the imaging step. The size of cells at the SC and granular layer was analyzed using the IMAGE/J software developed by the National Institute of Health (http://

rsb.info.nih.gov/ij/). Finally, the average grayscale intensity was calculated for each optical section (to minimize edge artifacts the central image area was used only) and normalized to the corresponding laser power. Thus, depth profiles of the backscattered light intensity could be constructed.

Cell Size Analysis

Corneocytes were removed from the skin surface at the upper inner arm, dorsal forearm, and thigh using adhesive tapes (D-Squames, CuDerm Corporation, Dallas, TX). Each tape was applied uniformly on the skin and was removed after 1 min. Images of the removed corneocytes on the tapes were acquired using a video light microscope (HiScope Systems Co., Closter, NJ). The final image corresponded to an area of 2.7 mm × 2.1 mm. Images of individual cells were analyzed for cell area and perimeter using the IMAGE/J software.

Fluorescence Spectroscopy

To evaluate the keratinocyte proliferation rate the fluorescence ascribed to the tryptophan species was recorded (8–10). To this end, the skin sites of interest were examined in vivo using a fluorescence spectrophotometer (SPEX® SkinSkan, HORIBA Jobin Yvon Inc., Edison, NJ) equipped with a Xenon arc light source, double excitation and emission monochromators, and a bifurcated fiber-optic probe with a randomized distribution between excitation and collection fibers (diameter of each fiber: 200 μm). A detailed description of the instrumentation is given elsewhere (12). Before each set of measurements the instrument was spectrally calibrated for excitation and emission in the region 250–650 nm. The chromatic resolution of the spectrofluorimeter was ± 2 nm. Measurements were performed by placing the fiber optic probe in contact with the skin site of interest and recording the excitation spectra in the range from 240 to 320 nm with emission set at 340 nm (tryptophan excitation maximum at 295 nm). The tryptophan fluorescence signal was normalized to the 390 nm excitation band to minimize the effect of instrumental parameters on the measurements (11).

Statistics

All data are presented as average ± one SE of mean except otherwise noted. Comparisons between infant and adult skin data were performed using Student's *t*-test where applicable and ANOVA test otherwise.

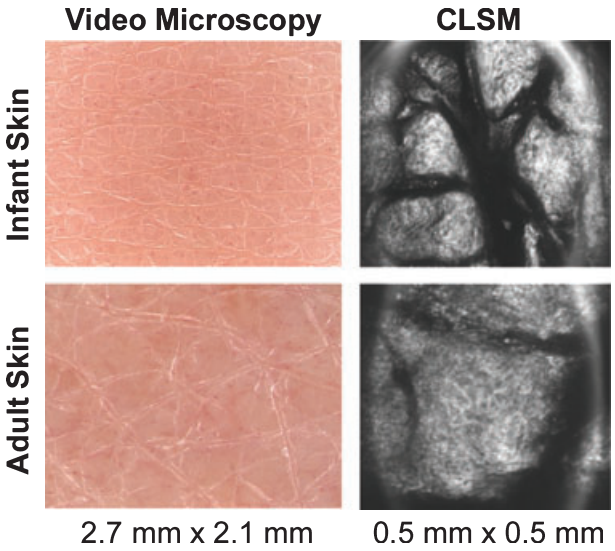

Figure 1. The skin surface appears different between infants and adults. Examples are shown of in vivo video microscopy and confocal laser scanning microscopy images of the surface of infant and adult skin. Infant skin appears to have a denser network of microrelief lines than adult skin. The stratum corneum "island" structures are flatter and larger in adult skin.

Statistical significance was accepted at the level of $p < 0.01$.

RESULTS

Infant Skin Surface Is Different than Adult

Both video microscopy and CLSM images demonstrated striking differences between adult and infant skin surface (Fig. 1). In infants, the network of microrelief grooves appears to be denser (more lines per projected area) and the intra-relief "island" structures appear to be more rounded and plump. In contrast, these structures in adults appear to be flatter and with larger surface area. Moreover, in adults, the edges of these structures are more distinct in video microscopy images. This increase in contrast may be attributed to the dryer condition of the corneocytes at these sites. Infant skin on the other hand appears to be well hydrated in accordance with the skin moisturization measurements previously reported (3). Surprisingly, the depth of the glyphics as measured in the CLSM images was found to be the same in adult and infant skin (~90 μm).

Infant Skin Architecture Is Different than Adult Beneath the Surface

In vivo CLSM images revealed differences between adult and infant epidermis (Fig. 2). The projected area of

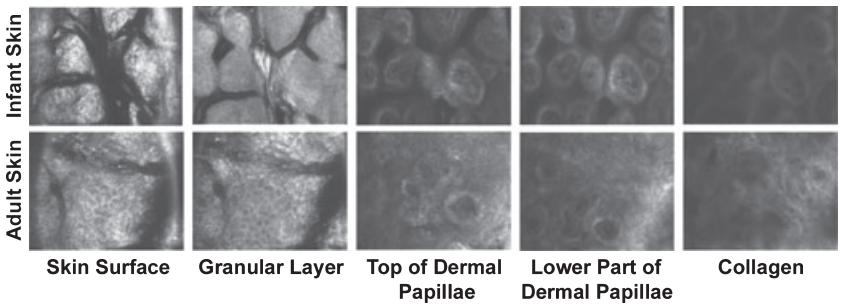

Figure 2. In vivo confocal laser scanning microscopy reveals differences between adult and infant skin beneath the skin surface. Representative images are shown of different layers through the skin. The one-to-one relationship of the papillae to the stratum corneum surface structures is evident in infant skin and not in adult. Also the overall brighter signal at the collagen level in adult skin is characteristic of thicker collagen fibers in adult skin.

dermal papillae displays a fairly homogeneous size distribution in infant skin, whereas in adults, the dermal papillae vary in size and are more irregular in shape. Interestingly, in infant skin, there appears to be a one-to-one relationship between the intra-glyph "island" structures at the surface and the underlying dermal papillae at the bottom of the epidermis, possibly indicating a single structural unit relationship. This relationship is absent in adult skin, where a single surface "island" may correspond to several papillae underneath.

Infant SC and Supra-Papillary Epidermis Are Thinner than Adult

Infant SC thickness calculated from in vivo CLSM images is on average 30% lower than that of adult, whereas the infant supra-papillary epidermis was found to be on average 20% thinner than that of adults (Table 1).

TABLE 1. *Comparison of structural parameters between infant and adult skin. The stratum corneum and supra-papillary epidermis are thinner in infant skin compared to adult skin. Infant corneocytes are smaller than adult in all three areas where samples were collected (upper inner arm, dorsal forearm, and upper thigh area). Infant cell at the granular layer are smaller compared to adult. Infant cell density at the granular layer is higher than adult. All differences between infants and adults are statistically significant. Data are shown as average ± one standard deviation*

	Infant skin	Adult skin
Stratum corneum thickness (μm)	7.3 ± 1.1	10.5 ± 2.1
Supra-papillary epidermal thickness (μm)	29.7 ± 3.4	36.2 ± 5.2
Corneocyte size (μm^2)		
Upper inner arm	949.9 ± 19.1	1077.6 ± 26.9
Dorsal forearm	907.3 ± 23.4	1071.0 ± 25.7
Thigh	953.0 ± 23.8	1154.4 ± 33.7
Granular cell size (μm^2)	443.6 ± 6.2	475.9 ± 8.3
Granular cell density (cells/mm^2)	1577.8 ± 45.4	1382.6 ± 37.4

Infant Corneocytes and Granular Layer Keratinocytes Are Smaller than Adult

Corneocyte size was evaluated by image analysis of adhesive tapes removed from the skin sites of interest (Fig. 3). In all sites examined (upper inner arm, dorsal forearm, and lower thigh), the size of infant corneocytes was found to be smaller than that of adult (Table 1). No differences were noticed in corneocyte size among the three sites examined for either adults or infants. The differences between adult and infant keratinocyte size were measurable to a lesser but still significant level at the granular layer (Fig. 4, Table 1). Interestingly, both infant and adult keratinocytes undergo on average a doubling of their projected area as they transform from granular cells to corneocytes. Cell densities in the granular (but not the corneal) layer could also be measured form the confocal data and are shown in Table 1. The smaller cell size in infants is often thought to be due to higher cell turnover rates. We confirmed that this is the case using in vivo fluorescence spectroscopy (Fig. 5). These data also show that there appears to be a progressive decrease in the epidermal cell proliferation rate during the first year of life.

The Border Between Papillary and Reticular Dermis May Be Observed in Adults

Confocal laser scanning microscopy reflectance intensity profiles decrease in an exponential-like manner because of light losses by scattering. In the case of adult skin, the monotonic decay is interrupted by a local plateau at around 100–140 μm, which is absent in the profiles of infant skin (Fig. 6). This plateau has previously been ascribed to the border between papillary and reticular dermis (13). Collagen and elastic fibers in the reticular

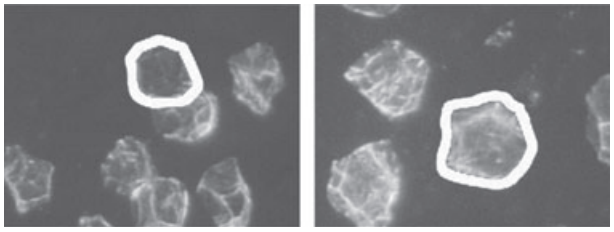

Figure 3. Infant corneocytes are smaller than the adult ones. Representative video microscopy images of corneocytes removed by tape stripping from infant and adult skin.

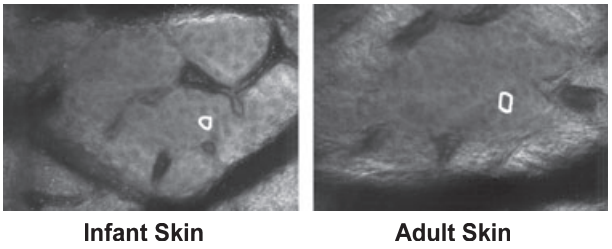

Figure 4. Infant granular cells are smaller than the adult ones. Representative confocal laser scanning microscopy images at the depth where granular cells can be observed from infant and adult skin.

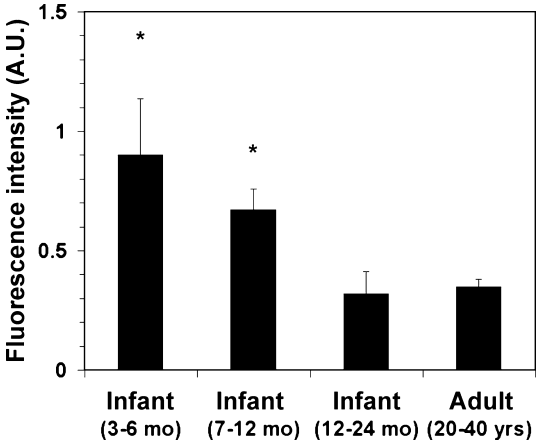

Figure 5. The epidermal cell proliferation rate in infants is higher than adults. The intensity of the tryptophan band (295 nm excitation) was measured using in vivo fluorescence excitation spectroscopy. The star (*) indicates statistical significance between this infant group and the adult group.

dermis are thicker than those of the papillary layer and are expected to increase locally the reflected signal. This feature was absent in the data from infant skin, confirming the published observation that the collagen bundles of the upper reticular dermis are not as thick in infants as in adults (14,15) and therefore the transition

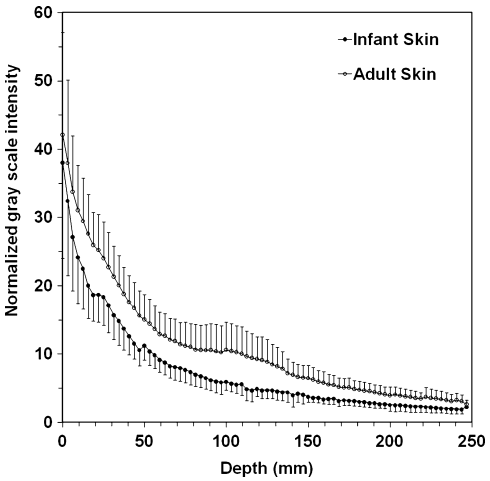

Figure 6. Confocal laser scanning microscopy shows that the border between papillary and reticular dermis (shoulder between 90 and 140 μm depth) can be observed in adult skin, but is absent in baby skin. The gray level intensity profiles for the confocal stacks are given as average values normalized to the laser power used at the corresponding depth. Data are given as mean ± one SD.

between papillary and reticular dermis is more gradual in infants. Note that the small shoulders present in the infant data are attributed to noise.

DISCUSSION

During the first year of life, skin has been shown to be in a state of active development, in particular with regard to its water handling properties (3,15–17). Such functional differences between infant and adult skin may arise at least in part from differences in microstructure. In this study, we examined the morphology of infant and adult skin in vivo at the microscopic level. We observed differences in microglyph density, cell size, epidermal layer thickness, dermal structure, and density of papillae. On the other hand, some striking similarities exist, as for example, the glyphic structures perceived on the surface of the SC have the same depth in infant and adult skin. Moreover, we report for the first time a structural relationship between papillae and skin surface that exists in infant skin and disappears later in life.

In utero epidermal maturation occurs continuously. Functional maturation of the SC begins in the third trimester of gestation. By 34-weeks gestational age the epidermis has largely matured: the SC and the dermo-epidermal undulations become visible (18). However, skin structures at the organ level continue to evolve even after birth. During the first 3 months of life, skin roughness decreases correlating with a concomitant increase in SC hydration (19), although this may not be

the only reason. Moreover, scanning electron microscopy revealed 10 times more hair structures per unit skin surface area in newborns compared with adults (20).

Infant corneocytes have been reported to be thicker (in height) than adult (21). The size of corneocytes shed from the horny layer has been suggested as an indication of the proliferation rate of the epidermal keratinocytes: smaller size indicating faster proliferation (22). Detailed three-dimensional morphometry using atomic force microscopy showed that although adult corneocytes are flatter than infant, the total volume remains statistically similar between the two groups (21). In accordance with these reports, our data also illustrate that the infant corneocyte, as well as granular keratinocyte, projected area is smaller than the adult and we confirm the higher proliferation rate in infants using an intrinsic fluorescence marker of epidermal cell proliferation (9).

It has been reported that morphologically there is increasing epidermal cellularity and undulation of the rete ridges at the dermo-epidermal junction in neonates and young infants (18). Our data corroborate these results. Beyond these observations, we observed in infants a direct relationship between the dermal papillae structures at the bottom of the epidermis and the intra-relief areas of SC at the surface. There appears to be a structural unit in infant epidermis that potentially points to a common precursor proliferative unit at the basal layer. This one-to-one relationship between epidermal structures is lost in adults possibly implicating both chronological aging and photoaging processes. Alternatively, the loss of the one-to-one relationship in a growing organism may develop with the original epidermal units controlling a greater area with more dermal papillae.

No consensus in the literature for the comparison in terms of skin thickness between infants and adults was observed. While a pulsed ultrasound study showed that infant skin is thinner than adult skin (23) and a second study showed that there was a slight increase in the number of SC layers with age in the skin of the cheek and back (24), another report stated that the thickness of their SC is not significantly different and therefore cannot be used to explain differences in percutaneous absorption (25). Such discrepancies may be attributed to variations in histological preparations. Ex vivo SC can have very different appearance particularly when prepared for histology. Using in vivo methods, we show that both the SC and the supra-papillary epidermis are thinner in infant skin compared with adult. Furthermore, the SC thickness calculated in this study for adult subjects is within the range of reported thicknesses calculated from in vivo CLSM data: 8–14 μm depending on body site (5).

Histometric measurements by in vivo CLSM comprise a sensitive and noninvasive tool for characterizing and quantifying histological changes in the epidermis and papillary dermis as a result of aging (26). Age-related effects on epidermal structures have been studied in adults using noninvasive in vivo methods such as ultrasound [for a review see (27)], optical coherence tomography (OCT) (13,28), and CLSM (13,26). Ultrasonography has been reported to give variable results concerning the measurement of skin thickness (27) and the only parameter that can be extracted from OCT is equivalent to a similar parameter measured from CLSM image analysis (13). Therefore of the three in vivo methods, more information can be obtained from CLSM, which is taking the place of a ''golden standard'' for in vivo micro-structural measurements.

Skin surface morphology has long been recognized as reflecting skin pathology. In a study on hairless mice, skin surface roughness was found to be associated with both water content and thickness of SC (29). Infant micro-relief lines were found to be denser than adult, which implies a larger surface per projected area. This in turn may explain at least in part the differences between infant and adults skin in terms of water absorption and desorption (3).

Moreover, although infant SC has higher TEWL rates than adult, it also has higher water content as shown both by capacitance measurements and by in vivo Raman microspectroscopy (3). This is not necessarily a contradiction as TEWL values can be independent of the water content of the SC reservoir as long as the influx-outflux equilibrium of water in the SC can support the high values of water content. Interestingly, the plateau level in the water concentration profile calculated by the Raman method (marking the beginning of viable epidermis) is reached 5–10 μm earlier in infant SC than in adult. This observation confirms the finding of the current study that infant SC is thinner, keeping in mind that cross study comparisons should be made with caution.

In conclusion, infant skin continues to change and develop during the first years of life. We report that compared with adult skin, infant microrelief structures are denser, SC and supra-papillary dermis are thinner, dermal papilla size is more uniform, corneocyte and granular cell size are smaller. In addition, we observed a one-to-one relationship between papillae and surface structures in infant skin exclusively and a distinct papillary-to-reticular dermis transition in adult skin only. Previous reports on differences in skin thickness, skin pH, and SC hydration levels between newborn and adult skin show that neonatal skin is always adjusting to the extra-uterine environment (1). In the light of the findings of this article as well as our previous report (3), we can extend the above statement to infants through at least their first year of life.

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CONFLICT OF INTEREST

All authors are employees of the Johnson & Johnson family of companies as indicated by their affiliations.

REFERENCES

1. Chiou YB, Blume-Peytavi U. Stratum corneum maturation. A review of neonatal skin function. Skin Pharmacol Physiol 2004;17:57–66.
2. Mancini AJ, Kaulback K, Chamlin SL. The socioeconomic impact of atopic dermatitis in the United States: a systematic review. Pediatr Dermatol 2008;25:1–6.
3. Nikolovski J, Stamatas GN, Kollias N et al. Barrier function and water-holding and transport properties of infant stratum corneum are different from adult and continue to develop through the first year of life. J Invest Dermatol 2008;128:1728–1736.
4. Selkin B, Rajadhyaksha M, Gonzalez S et al. In vivo confocal microscopy in dermatology. Dermatol Clin 2001;19:369–377.
5. Huzaira M, Rius F, Rajadhyaksha M et al. Topographic variations in normal skin, as viewed by in vivo reflectance confocal microscopy. J Invest Dermatol 2001;116:846–852.
6. Gonzalez S, Swindells K, Rajadhyaksha M et al. Changing paradigms in dermatology: confocal microscopy in clinical and surgical dermatology. Clin Dermatol 2003;21:359–369.
7. Branzan AL, Landthaler M, Szeimies RM. In vivo confocal scanning laser microscopy in dermatology. Lasers Med Sci 2007;22:73–82.
8. Brancaleon L, Lin G, Kollias N. The *in vivo* fluorescence of tryptophan moieties in human skin increases with UV exposure and is a marker for epidermal proliferation. J Invest Dermatol 1999;113:977–982.
9. Doukas AG, Soukos NS, Babusis S et al. Fluorescence excitation spectroscopy for the measurement of epidermal proliferation. Photochem Photobiol 2001;74:96–102.
10. Kollias N, Gillies R, Moran M et al. Endogenous skin fluorescence includes bands that may serve as quantitative markers of aging and photoaging. J Invest Dermatol 1998;111:776–780.
11. Stamatas GN, Estanislao RB, Suero M et al. Facial skin fluorescence as a marker of the skin's response to chronic environmental insults and its dependence on age. Br J Dermatol 2006;154:125–132.
12. Stamatas GN, Wu J, Kollias N. Non-invasive method for quantitative evaluation of exogenous compound deposition on skin. J Invest Dermatol 2002;118:295–302.
13. Neerken S, Lucassen GW, Bisschop MA et al. Characterization of age-related effects in human skin: a comparative study that applies confocal laser scanning microscopy and optical coherence tomography. J Biomed Opt 2004;9:274–281.
14. Vitellaro-Zuccarello L, Cappelletti S, Dal Pozzo Rossi V et al. Stereological analysis of collagen and elastic fibers in the normal human dermis: variability with age, sex, and body region. Anat Rec 1994;238:153–162.
15. Holbrook KA. A histological comparison of infant and adult skin. New York: Marcel Dekker, Inc., 1982.
16. Visscher MO, Chatterjee R, Munson KA et al. Changes in diapered and nondiapered infant skin over the first month of life. Pediatr Dermatol 2000;17:45–51.
17. Visscher MO, Chatterjee R, Ebel JP et al. Biomedical assessment and instrumental evaluation of healthy infant skin. Pediatr Dermatol 2002;19:473–481.
18. Evans NJ, Rutter N. Development of the epidermis in the newborn. Biol Neonate 1986;49:74–80.
19. Hoeger PH, Enzmann CC. Skin physiology of the neonate and young infant: a prospective study of functional skin parameters during early infancy. Pediatr Dermatol 2002; 19:256–262.
20. Marchini G, Nelson A, Edner J et al. Erythema toxicum neonatorum is an innate immune response to commensal microbes penetrated into the skin of the newborn infant. Pediatr Res 2005;58:613–616.
21. Kashibuchi N, Hirai Y, O'Goshi K et al. Three-dimensional analyses of individual corneocytes with atomic force microscope: morphological changes related to age, location and to the pathologic skin conditions. Skin Res Technol 2002;8:203–211.
22. Grove GL, Kligman AM. Corneocytes size as an indirect measure of epidermal proliferative activity. In: Marks R, Plewig G, eds. Stratum corneum. Berlin: Springer-Verlag, 1983:191–195.
23. Tan CY, Statham B, Marks R et al. Skin thickness measurement by pulsed ultrasound: its reproducibility, validation and variability. Br J Dermatol 1982;106:657–667.
24. Ya-Xian Z, Suetake T, Tagami H. Number of cell layers of the stratum corneum in normal skin – relationship to the anatomical location on the body, age, sex and physical parameters. Arch Dermatol Res 1999;291:555–559.
25. Fairley JA, Rasmussen JE. Comparison of stratum corneum thickness in children and adults. J Am Acad Dermatol 1983;8:652–654.
26. Sauermann K, Clemann S, Jaspers S et al. Age related changes of human skin investigated with histometric measurements by confocal laser scanning microscopy in vivo. Skin Res Technol 2002;8:52–56.
27. Waller JM, Maibach HI. Age and skin structure and function, a quantitative approach (I): blood flow, pH, thickness, and ultrasound echogenicity. Skin Res Technol 2005;11:221–235.
28. Gambichler T, Matip R, Moussa G et al. In vivo data of epidermal thickness evaluated by optical coherence tomography: effects of age, gender, skin type, and anatomic site. J Dermatol Sci 2006;44:145–152.
29. Sato J, Yanai M, Hirao T et al. Water content and thickness of the stratum corneum contribute to skin surface morphology. Arch Dermatol Res 2000;292:412–417.