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Infant Skin Maturation: Preliminary Outcomes for Color and Biomechanical Properties

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Abstract

Background—Newborn infant skin changes after birth but studies have focused on the epidermal barrier. Dermal properties are relevant for care, but literature on postnatal changes is sparse. We further characterized skin maturational changes in lightness, color and response to biomechanical stress.

Methods—Normal skin sites from subsets of participants in a trial on the progression and stage of infantile hemangiomas were retrospectively examined. Standardized photographs were analyzed as L*, a* and b* images. Biomechanics were measured with the Cutometer®.

Results—Color changed significantly with increasing age. Skin was darker and redder at 2.0 versus 5.4, 8.5 and 12.8 months. Yellow color increased, with higher values at 12.8 versus 2.0, 3.5 and 5.4 months. Chest tissue was consistently more elastic than arm and face sites, with significantly higher elasticity for the youngest and oldest age groups. Biological elasticity, elastic recovery and total recovery were significantly greater for the oldest subjects. Viscoelasticity and elastic deformation were lower at 5.5 versus 8.8 and 17.6 months. Arm viscoelastic creep was highest at 2.8 months.

Conclusion—Skin maturation continues into year two. Increasing elasticity and decreasing viscoelasticity may reflect increased collagen structure/function. The findings have implications for prevention of skin injury associated with mechanical forces.

Keywords

skin; infant; lightness; red color; yellow color; biomechanical properties; elasticity; deformation; elastic recovery; objective measurement

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Introduction

Full term newborn infant skin has a thick epidermis, well-formed stratum corneum (SC), and low transepidermal water loss, indicating a highly effective barrier (1). It undergoes maturational changes for months after birth, including a rapid decrease then increase in SC hydration, decreasing surface acidity with acid mantle development and appearance of functional toll-like receptors (TRP3, during gestation and postnatally) for innate immunity (2–5). Infant skin maturation studies have generally focused on epidermal barrier changes.

Objectively measured skin color differentiated illness severity in NICU patients. Infants of high severity had significantly lower b^* values, i.e., more yellow color, than less ill infants (6). Skin lightness over postnatal day 1 was highly correlated with gestational age (7). Yellow skin color was highly correlated to serum bilirubin among 2441 premature and full term infants and more reliable than visual assessment (8).

Dermally based skin properties, such as tissue mechanics, color, and pigmentation, are relevant for infant care. The microvasculature continues to evolve for about 4 months (9). The SC and epidermis are 30% and 20% thinner at 6 – 24 months versus adults, with no distinct epidermal-dermal border (10). Surface dermatoglyphics are denser and dermal papillae more uniform. Premature infant dermis is deficient in structural proteins and easily torn (11). Repeated ischemia and reperfusion from mechanical trauma causes pressure injuries. For example, pressure related nasal trauma occurred in 42% of NICU patients using continuous positive airway pressure and the risk was greater for infants < 32 weeks gestational age (12). Implementation of strategies to prevent pressure injuries is a high priority in pediatric care.

Dermal fibrous collagen and elastin networks, epidermis and subcutaneous tissue give rise to the biomechanical properties of skin. When measured with suction device and 6 mm probe, they are due to the dermis (13). Property ratios, such as biological elasticity (U_r/U_f), are thickness independent (14). In adults, biomechanical properties vary with body site and age (15–17). Elasticity decreased over 20 – 60 years, but was lower for 10 – 20 than 20 – 30 and 30 – 40 years (18). Biological elasticity, overall elasticity and total deformation decreased over time and site for 20–29, 30–39, 40–49, 50–59, 60–69, 70–85 years (19).

The literature on postnatal dermal changes is sparse, as most of the structural, histological and compositional research has been on fetal versus adult skin and not on newborns. We aimed to further characterize infant skin maturational changes in color and biomechanics via a descriptive, retrospective study on normal skin from data collected in a trial to assess the progression infantile hemangiomas (20–22). The parent trial: a) quantified hemangioma features of color, size, and volume and responses to thermal and mechanical stress, b) evaluated changes in hemangiomas over time (age) and with treatment, c) compared quantitative measures to clinical state, and d) established a quantitative database for hemangiomas. Uninvolved contralateral skin sites were measurement controls. The control site data provides an opportunity to quantify changes over time, i.e., maturational effects, in normal infant skin. We report quantitative of skin lightness, color, and response to mechanical stress over time using standardized digital imaging and biomechanical methods.

Methods

Subjects

The study was conducted among two subsets of patients from the Hemangioma and Vascular Malformation Center enrolled in a trial to quantify the progression of infantile hemangiomas over time and relative to clinical stage (20–22). The Institutional Review Board approved the protocol and parents/guardians provided written informed consent.

Experimental Design

Per the parent trial, subjects had skin evaluations at scheduled clinic visits, typically every 1–2 weeks to establish therapeutic dose, then every 1–2 months followed by longer intervals. Uninvolved skin sites contralateral to the hemangioma were examined.

Color Imaging and Analysis

Subjects acclimated to room conditions for at least 15 minutes and were maintained in a calm state. High resolution digital color images were collected at 30 cm perpendicular to the contralateral uninvolved skin site (Nikon D90 12.3 megapixels, Micro Nikkor 60-mm lens, cross polarization, and Nikon R1 Wireless Close-Up flash, Nikon Corporation, Tokyo, Japan) (23). Images were taken with standardized conditions (lighting, subject position), at a fixed distance, and with polarized light (24) and standardized for white balance and color (23). Images were color corrected (Machbeth color card), converted from RGB (to CIE Lab color space, and separated into L* (dark-light), a* (green-red) and b* (blue-yellow) channel images (ImageJ, NIH, Washington, DC, USA) (23). Mean lightness, red color and yellow color values were reported on 0 – 255 intensity scales.

Biomechanical Properties

Biological elasticity (Ur/Uf), overall elasticity (Ua/Uf), net elasticity (Ur/Ue), viscoelasticity (Uv/Ue), elastic recovery (Ur), residual deformation (R), total recovery (Ua), viscoelastic creep (Uv), elastic deformation (Ue), and total deformation (Uf) were measured with a Cutometer® 575 (Courage & Khazaka electronic GmbH, Koln, Germany), 6-mm probe aperture, 2 second 200 mbar negative pressure and 2 second relaxation.

Statistical Analysis

Skin lightness, red color, and yellow color were analyzed over five time points (mean age at evaluation) with univariate general linear models (GLM) with $p < 0.05$ (SPSS v21, SPSS, Inc., Chicago, IL) with regards to treatment. Biomechanical properties were evaluated in two ways: (1) by body site, with treatment and/or age in the model and (2) over time (mean age at evaluation) by body site. Post-hoc pairwise comparisons were made using the least significant difference. The relationships between tissue properties and age were examined with correlation methods.

Results

Subjects

For hemangioma trial subjects ($n = 119$), the number of clinic visits (measurement sessions) varied with treatment plan. The youngest subjects with multiple visits were selected to adequately assess maturational changes. The sites, dictated by the hemangioma locations, were chest, leg, arm, back and face.

Skin Color – Effects Over Time

Skin color over time was evaluated for 16 subjects and 21 sites, with a median of 4 visits per subject (range 2–5) to generate 79 color measurements. Mean ages were 2.0 ± 0.5 months at visit 1 to 12.8 ± 2.1 months at visit 5 (Table 1). There were 12 females and 4 males, reflecting the female-predominant occurrence of hemangiomas (25). The majority ($n = 13$) received oral propranolol, one had topical timolol and two were untreated.

Skin lightness (L) increased, red color (a^*) decreased, and yellow color (b^*) increased, i.e., blue color decreased. The skin was lighter at 12.8 versus 2.0 and 3.5 months and at 5.4 and 8.5 versus 2.0 months ($F = 3.6$, $p = 0.009$) (Figure 1a). Red color was higher at 2.0 months than any other time and higher at 2.0 and 3.5 versus 12.8 months ($F = 5.6$, $p = 0.001$) (Figure 1b). Yellow color was lower at 2.0 and 3.5 versus 5.4 and 12.8 months and lower at 5.4 than 12.8 months ($F = 9.2$, $p < 0.001$) (Figure 1c).

Biomechanical Properties

Subjects and Analysis Strategy—Biomechanical properties could not be determined at every visit due to subject intolerance of the procedure on occasion. Subjects with a least 2 visits were included. There were 28 subjects and 31 sites with 3 visits per subject (median, range 2–6) yielding 98 evaluations. There were 18 females and 10 males. Eighteen received propranolol, 3 had timolol and 7 were untreated.

Initially, the effect of body site was determined using all evaluations and age as a covariate (GLM). The sites differed significantly ($p < 0.05$) for biological elasticity (Ur/Uf), overall elasticity (Ua/Uf), net elasticity (Ur/Ue), elastic recovery (Ur), and total recovery (Ua) (data not shown). As pairwise comparisons showed no differences for (a) chest versus leg and (b) arm versus back, site data were combined.

The data were grouped by age at assessment, originally into 5 categories to align with ages for the color evaluations. Due to limited observations for the youngest group (less than 3 months), the data were distributed in four groups. Mean ages were 3.1 ± 0.9 months (youngest) to 16.6 ± 3.4 months (oldest group) (Table 2). As expected from the study design, sample sizes varied by site and age group (Table 2).

Effect of Site by Age Group—Biomechanical properties differed by site (Supplementary Table 1). (1) At 3.1 months, biological elasticity (Ur/Uf) was significantly higher for chest versus arm and face (Figure 2a). Net elasticity (Ur/Ue) and elastic recovery (Ur) were higher for chest versus face. Viscoselasticity (Uv/Ue) and viscoelastic creep (Uv) were higher for arm than face. (2) Chest, arm and face sites were not different at 5.5 months. (3) Total

recovery (U_a) at 8.8 months was higher for chest than arm and face (Figure 2b) while elastic recovery (U_r), elastic deformation (U_e) and total deformation (U_f) were higher for chest versus arm. (4) For 16.6 months, total recovery (U_a) differed significantly for all sites, i.e., highest for chest and lowest for face (Figure 2b). Biological elasticity (U_r/U_f), net elasticity (U_r/U_e), and elastic recovery (U_r) were higher for chest than arm and face. Overall elasticity (U_a/U_f) was higher at both chest and arm than face. Elastic (U_e) and total (U_f) deformation were higher at chest versus face.

Effect of Age by Site—Biomechanical properties differed significantly with age (Supplementary Table 2). (1) For chest sites, biological elasticity (U_r/U_f), elastic recovery (U_r) and total recovery (U_a) were significantly higher at 16.6 months versus 3.1, 5.5 and 8.8 months. Viscoelasticity (U_v/U_e) was higher at 5.5 than 3.1, 8.8 and 16.6 months. Elastic deformation (U_e) was lower at 5.5 than 16.6 months. (2) For arm sites, only viscoelastic creep (U_v) differed significantly, with lower values at 5.5 and 8.8 months versus 3.1 months. (3) Face site biomechanical properties did not vary with age.

Moderate, significant positive correlations were found with age for chest site elastic recovery (U_r) (Figure 3), biological elasticity (U_r/U_f), total recovery (U_a), elastic deformation (U_e), net elasticity (U_r/U_e) and total deformation (U_f) (Table 3). Age correlated negatively to viscoelastic creep (U_v) for arm sites.

Discussion

Newborn infants rely on their skin to provide structural integrity, resistance to mechanical trauma, thermal regulation, and sensory transduction, among other functions. The study results demonstrate functional skin maturation during neonatal and young infancy, continuing into the second year. To our knowledge, this is the first report describing changes in skin color and biomechanics over the first years of life.

We retrospectively examined normal sites among a subset of infants aged 1.3 to 16.9 months from a clinical trial to quantify hemangioma progression and clinically determined stage (20). Infants had darker skin at 2.0 months than at 5.4, 8.5 and 12.8 months (Figure 1a). Red color was higher at 2.0 months than any other time (Figure 1b). Yellow color increased, with higher values at 12.8 versus 2.0, 3.5 and 5.4 months (Figure 1c).

Previous reports indicated varying skin color over 25–44 weeks gestational age. The dark red color in premature infants was attributed to blood and vasculature visible through thin, translucent skin, changing to pink as thickness increased (26). Pigmentation decreased as gestational age increased from 37 to 42 weeks (27). Further increases over postnatal days 25–75 were observed only in African American premature infants (28). Ultraviolet-induced pigmentation was very low for 6–24 month infants during their first summer but significantly higher a year later, suggesting darkening over the period (29). Hemoglobin was not measured, but levels are generally constant for our age range (30) and not likely a cause of higher redness at 2 months. By confocal laser scanning microscopy, infant skin had an intricate microvasculature network 4–7 days after birth that was progressively farther from

the skin surface over 1, 3 and 6 months (31). Vasculature closer to the skin surface may account for the higher red color at 2.0 months.

Tissue response to mechanical stress varied significantly with body site. Chest tissue was consistently more elastic than arm and face sites and significantly higher for the youngest and oldest age groups (Figure 2, Table 3, Supplementary Table 1, 2). Our higher U_r/U_f for chest versus arm and face are generally consistent with reports for adults, i.e., higher at abdomen, thigh and upper arm versus back and lowest at forehead (16, 19). However, U_r/U_f was significantly *lower* in older versus younger adults at forearm and back (16). Elasticity was significantly higher at chest sites versus forearm, hand and finger in normal adults (32). Significantly higher elasticity, viscoelasticity and extensibility occurred in females aged 25–64 years for the neck versus cheek and forearm (ventral) (33). Elasticity was related (negatively) to age for the neck only.

We observed significant effects of age group, particularly for the chest, with greater biological elasticity (Figure 2a), elastic recovery and total recovery (Figure 2b) for the oldest subjects. In contrast, viscoelasticity and elastic deformation were lower for the younger group at 5.5 compared to 8.8 and 17.6 months (Supplementary Table 2). The arm site reflected less elastic skin, i.e., greater viscoelastic creep, for the youngest infants at 2.8 months versus those of 5.5 and 9.3 months (Supplementary Table 2).

Collectively, the findings suggest that infant skin becomes more elastic by the second year and is more viscoelastic in early infants, i.e., first 3–4 months. However, body site significantly influences tissue biomechanics. The generally higher values for the chest permitted differentiation with age. Comparative studies are sparse as previous reports have largely focused on older subjects. Our results are consistent with a report of significantly greater skin elongation/extensibility in infants (< 12 months) than any other age group, i.e., 1–2, 3–5, 6–8, 9–11, 12–14, 15–19, 20–29, 30–40 and > 50 years (34). The skin tension/extension ratio decreased initially from ~ 2 – 10 years, with lowest values for 15 – 25 years, then increased (2 – 67 years) (35). Skin thickness at the shoulder (deltoid) increased from 1.6 mm at 2 months to 1.84 mm at six months (36). By confocal microscopy, dermal papillae were not visible at 4–7 days but developed during the first three months, suggesting a more complex dermal structure (31). Our increases in chest U_r , U_a , and U_e and reduction in arm U_v with increasing age may be impacted by maturational changes in skin thickness and structure.

Our increases in biological elasticity (U_r/U_f) may reflect elevation in collagen, since the reported changes in reticular collagen parallel the alterations in U_r/U_f . Neonatal dermis is “between” fetal and adult for fiber bundle thickness, size and composition (37). Less structured fetal/neonatal dermis has higher cell differentiation and higher turnover rate than adults (38). Low total collagen is sustained for 10–15 postnatal days (rat model), suggesting persistence of fetal forms (39). Fibrous connective tissue is produced in large quantities after birth (40). Collagen increases rapidly from birth to month two, further to one year and decreases by two years (41). Infant collagen bundles are less dense than adults (42). During development and activity, mechanical forces experienced by the skin are converted to biochemical reactions via mechanotransduction (43). Mechanical stress increases dermal

collagen fibril diameter and decreases fibril density versus non-stressed skin without changing dermal thickness (44). It is possible that mechanotransduction facilitates dermal maturation postnatally.

Nearly 80% of the NICU pressure injuries were due to pressure from medical devices and occurred 4–6 weeks after admission, i.e. in ages comparable to our youngest subjects (45). The reduced biological elasticity, elastic recovery, and total recovery in the youngest subjects may prevent restoration from repeated pressure cycles and thereby increase pressure injury risk. The *in vivo* biomechanical data from this study may enhance finite element models for device-related stress since current models are from animal measurements due to lack of human data (46).

Specific features of this study were noteworthy, as they emphasize potential limitations. The frequency and time between evaluations were not standardized, i.e., dictated by treatment plan versus consistent intervals. This variation necessitated classification into age strata to assess effects over time. Consequently, the groups were composed of different individual subjects. Hemangioma treatment effects on uninvolved sites are unknown, therefore, it was included in the statistical model. Furthermore, location of the skin sites varied by age and number of evaluations. We analyzed the data in two ways in an attempt to control for site and age. We were unable to measure skin thickness. Noninvasive characterization of skin thickness, composition and structure, e.g., confocal microscopy is warranted to fully explain the observed maturational changes in thickness-dependent properties, i.e., U_f , R , U_a , U_r , U_e , and U_v .

Nevertheless, the biomechanical response to stress, coupled with quantitation of skin lightness, red color and yellow color, extend previous reports that infant skin undergoes significant development well after birth. Though preliminary, the findings suggest that skin elasticity increases over the first years of life, may continue to increase until young adulthood and then decreases over time. The results have implications for skin care, particularly for hospitalized infants or those requiring treatment of cutaneous lesions. Previous reports showed that color (erythema) differences between capillary malformations, i.e., port wine stains, and normal skin predicted the treatment effectiveness and could guide treatment planning (47). Lower biological elasticity has implications for prevention and reduction of skin damage associated with mechanical forces, e.g. pressure injury from medical devices (48).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1 a,b,c.

Skin Color by Age Group

L values were higher, indicating lighter skin, at 12.8 versus 2.0 and 3.5 months and at 5.4 and 8.5 versus 2.0 months ($F = 3.6$, $p = 0.009$) (Figure 1a). Red color was higher at 2.0 months than any other time and higher at 2.0 and 3.5 versus 12.8 months ($F = 5.6$, $p = 0.001$) (Figure 1b). Yellow color was lower at 2.0 and 3.5 versus 5.4 and 12.8 months and lower at 5.4 than 12.8 months ($F = 9.2$, $p < 0.001$) (Figure 1c).

Figure 2 a,b.

Biomechanical Properties for Skin Sites by Mean Group Age.

Fig 2a. Biological elasticity (U_r/U_f) was significantly higher at the chest versus arm and face at 3.1 and 16.6 months. # Indicates significantly higher biological elasticity for chest versus arm and face sites. Fig 2b. Total recovery (U_a) was significantly higher for chest versus face at 8.8 months. All sites differed at 16.6 months with the highest values for chest and lowest for face. b. *Indicates all sites different. # Indicates significantly higher biological elasticity for chest versus arm and face sites.

Figure 3.

Chest Site Elastic Recovery Versus Age.

Moderate, significant positive correlations were found with age and some of the biomechanical properties. The relationship for chest site elastic recovery (Ur) is shown here.

Table 1

Demographic Characteristics: Color Features by Age at Visit

Visit	Number of Evaluations	Age (Months) Mean $\pm$ SD
1	21	2.0 $\pm$ 0.05
2	18	3.5 $\pm$ 0.06
3	17	5.4 $\pm$ 0.05
4	13	8.5 $\pm$ 1.0
5	10	12.8 $\pm$ 2.1
Total	79	---

Table 2

Mean Group Ages and Number of Evaluations by Body Site

Group	Age in Months mean $\pm$ SD (range)	Chest	Arm	Face	Total by Age
1	3.1 $\pm$ 0.9 (1.5 – 4.3)	6	18	8	32
2	5.5 $\pm$ 0.6 (4.6 – 6.8)	8	9	8	25
3	8.8 $\pm$ 1.6 (7.0 – 12.1)	12	12	4	28
4	16.6 $\pm$ 3.4 (12.6 – 22.0)	5	3	5	13
Total by Site	----	31	42	25	98

Table 3

Age correlations with skin biomechanical properties

Parameter	Site	r	p-value	n
Elastic recovery Ur	Chest	0.58	0.001	31
Total recovery Ua	Chest	0.50	0.004	31
Biological elasticity Ur/Uf	Chest	0.50	0.004	31
Elastic deformation Ue	Chest	0.49	0.005	31
Total deformation Uf	Chest	0.44	0.014	31
Net elasticity Ur/Ue	Chest	0.40	0.025	31
Viscoelastic creep Uv	Arm	-0.56	< 0.001	42