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Biomechanical Properties of Infantile Hemangiomas: Clinical Stage and Effect of Age

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Abstract

Background—Infantile hemangiomas (IHs) are benign vascular neoplasms with rapid capillary proliferation shortly after birth and slow involution with diminishing capillary proliferative activity, fibrosis and fatty replacement over 7 – 10 years.

Methods—Hemangiomas and contralateral control sites in eighty-eight subjects were measured with a suction device, 6-mm probe and 200 millibar negative pressure. Mechanical properties were assessed versus controls and effects of body site, depth, clinical stage, histology diagnosis and time.

Results—Biological elasticity, overall elasticity, net elasticity, total recovery and elastic recovery were lower for IH versus controls ($p < 0.001$). IH total deformation, elastic deformation, viscoelastic creep and residual deformation were higher than controls ($p < 0.001$). Involuting IHs had lower viscoelasticity than proliferating and stable lesions ($p < 0.001$) and lower viscoelastic creep than stable IHs ($p = 0.04$). IH viscoelasticity was higher at 2.3 than 12.9, 23.7 and 61.0 months and at 4.9 and 8.1 than 61.0 months. IH elastic recovery varied by body site with larger differences versus control for abdomen and leg. Elastic recovery differences from control were smaller at younger versus older ages.

Conclusions—Measurement of biomechanical properties may be useful to characterize IH progression and treatment response in clinical settings.

Keywords

skin; infant; infantile hemangioma; biomechanical properties; elasticity; deformation; elastic recovery; objective measurement; ontogeny

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Introduction

Infantile hemangiomas (IHs) are benign vascular neoplasms that undergo rapid capillary proliferation via excessive angiogenesis and/or vasculogenesis shortly after birth, followed by stabilization, and slow involution with diminishing cellular activity, apoptosis, increased fibrosis, regression of the capillaries and fibrofatty replacement over 7 - 10 years (1-5). Rapid growth occurs between 6-9 weeks (6), early proliferation before 3 months, most growth before 5 months, peak plateau around 7 months and involution after 10-12 months (7). IHs are more common in females and approximately 60% of IHs occur on the head and neck (1, 2). Up to 24% develop life- or function-threatening complications including ulcerations, hemorrhage, infection, vision impairment, airway obstruction, and disfigurement requiring treatment by multi-disciplinary specialist teams (8, 9). IHs are classified as superficial, deep, or mixed (majority of cases) based on the depth of dermal involvement (4, 10, 11). Deep tumors are soft, warm, slightly bluish and may proliferate for 2 years. Diagnosis is by history and examination of size, color, growth stage, tactile characteristics, and morphologic subtype.

Clinicians often palpate IHs to determine rigidity and evidence of fibrous/fatty tissue replacement as signs of involution. This suggests that IH viscoelastic properties may be related to lesion progression. Objective methods to assist clinicians in quantifying IH disease progression and treatment response are needed (12). We used standardized color imaging, three-dimensional surface imaging (height, volume) and dynamic infrared thermography to quantify IH disease progression from proliferation to involution, i.e., changes over time (13). To our current knowledge, we are not aware of any published studies that have investigated IH viscoelasticity with non-invasive biophysical methods as a way to determine and quantify disease progression.

The Cutometer® (Courage & Khazaka electronic GmbH, Köln, Germany) uses suction to quantify viscoelastic properties of skin *in-vivo* (14-17). Our group has found it useful in a variety of clinical settings (17-21). The objectives were to apply the Cutometer® to (1) quantify the biomechanical behavior of infantile hemangiomas relative to contralateral, normal skin, (2) relate the biomechanical properties to clinically assessed stage, body site, depth, size and histology, and (3) evaluate IH changes over time.

Materials and Methods

Subjects

The preliminary prospective observational cohort study was conducted among patients from the multidisciplinary Hemangioma and Vascular Malformation Center (HVMC) of Cincinnati Children's Hospital Medical Center between October 2011 and February 2013. Patients with superficial or mixed IH were eligible. Individuals with IHs in the diaper region or nasal tip were excluded due confounding effects or lack of a suitable control site, respectively. The Institutional Review Board approved the research and parents/guardians provided written informed consent.

Study Design

Clinicians assessed the IHs for color, size, temperature, tactile qualities (22), and assigned a stage as proliferating, stable or involuting and type (superficial, mixed, deep) at each clinic visit. Stage discrepancies were resolved by consensus. Demographic information, e.g., age, weight, gender, race, treatment, were recorded. Treated subjects were typically seen every 1-2 weeks initially, then at 1-2 months, followed by longer intervals. Untreated children were seen every 6 – 12 months. Clinicians decided treatment: propranolol (1-2 mg/kg per day), topical timolol (one drop 0.5% gel twice daily) (23) or untreated. Standardized high resolution color images were taken and IH volume and maximum height quantified with three-dimensional skin imaging and analysis, as previously described (13).

Biomechanical Measurements

Patients acclimated to room temperature and humidity for least 15 minutes before measurement. Biological elasticity (U_r/U_f), overall elasticity (U_a/U_f), net elasticity (U_r/U_e), viscoelasticity (U_v/U_e), elastic recovery (U_r), residual deformation (R), total recovery (U_a), viscoelastic creep (U_v), elastic deformation (U_e), and total deformation (U_f) were measured for the IHs (center of the lesion when possible) and contralateral control sites with a Cutometer® 575 (Courage & Khazaka electronic GmbH, Köln, Germany), 6-mm probe aperture, 2 second 200 mbar negative pressure and 2 second relaxation (mode 1) (Figure 1).

Histology

Hemangiomas were surgically removed, as dictated by the treatment plan. IH and controls were measured prior to surgery and compared with histology results. The pathologist reviewed the hematoxylin and eosin (H&E) stained sections to evaluate the morphologic features of the lesion, and confirmed the diagnosis with an erythrocyte-type glucose transporter protein (GLUT1) immunostain.

Statistical Analysis

Biomechanical properties of IH and controls were compared using univariate general linear models (GLM) procedures with age, body site and treatment as covariates (SPSS v21, SPSS, Inc., Chicago, IL). Effects with $p < 0.05$ were considered to be statistically significant. Measurements were analyzed by age at visit. Properties by clinical stage (proliferating, stable, involuting) were evaluated with control values, body site and treatment as covariates. Outcomes by IH depth (superficial versus mixed) were determined with control values, age and treatment as covariates. They were assessed by age group as a surrogate for time with control, anatomical location and treatment as covariates and post-hoc least significant difference (LSD) for pairwise comparisons. Effects of stage, depth and age group were also evaluated as difference between IH and control. Correlations among biomechanical, size and demographic characteristics were computed (i.e., Pearson, Spearman depending on normality).

Results

Subjects

Eighty-eight subjects participated with 67 females and 21 males. Age at first visit was 15.4 ± 22.2 months (range 1.3 – 144), 195 evaluations of 102 IHs and at least two visits for 34 subjects. There were 72 mixed, 24 superficial and 2 deep. Treatment was 55.3% propranolol (evaluation basis), 14.9% timolol and 29.7% untreated. The majority (34.3%) were on the face or head (Table 1). The IHs varied in size with mean volume of $6.2 \pm 8.4 \text{ mm}^3$ (range 0.01 – 57.0 mm^3) and mean height of $6.1 \pm 3.5 \text{ mm}$ (range 0.3 – 16.7 mm) for 172 evaluations.

Infantile Hemangioma versus Control Skin

Biological elasticity (U_r/U_f), overall elasticity (U_a/U_f), net elasticity (U_r/U_e), total recovery (U_a) and elastic recovery (U_r) were significantly lower for IH versus controls ($p < 0.001$) (Figure 2 a,b). Total deformation (U_f), elastic deformation (U_e), viscoelastic creep (U_v) and residual deformation (R) were significantly higher for IHs versus controls ($p < 0.001$) (Figure 2 a).

Effect of Body Site

For property difference (IH – control), significant body site effects were noted for elastic recovery, total recovery, elastic deformation, total deformation, residual deformation and biological elasticity (Table 2). Elastic recovery difference was higher for abdomen and leg and higher for head than all sites (Figure 3a). Biological elasticity difference was largest for abdomen and greater than arm, back, head and face. Differences in residual deformation and total recovery were larger for abdomen than face ($p < 0.05$). Body site variations occurred for IH properties with controls as covariates. IH net elasticity for head was lower than all sites and higher for leg versus arm, head and face and for abdomen versus arm and head ($p < 0.05$) (Figure 3b). Overall and biological elasticity were lower for head than all sites ($p < 0.05$) (Table 2). Viscoelasticity was lower for head than abdomen, leg, back and head and lower for arm versus leg and back ($p < 0.05$). Viscoelastic creep was lower for face than all sites ($p < 0.05$).

Superficial versus Mixed Hemangiomas

Viscoelasticity and viscoelastic creep were significantly higher for superficial versus mixed IHs ($p = 0.01$, $p = 0.002$, respectively). U_v/U_e was 0.22 (95% confidence interval 0.19 – 0.24) for superficial and 0.18 (95% confidence interval 0.16 – 0.19) for mixed IHs. U_v was 0.31 (95% confidence interval 0.27 – 0.34) and 0.24 (95% confidence interval 0.23 – 0.26) for superficial and mixed, respectively.

Effect of Clinically Assessed Stage

Viscoelasticity was lower for involuting than proliferating and stable IHs ($p < 0.001$). Viscoelastic creep was lower for involuting than stable IHs ($p = 0.04$) (Figure 4). Elastic recovery tended to be lower for stable than involuting but did not reach significance ($p = 0.051$).

Effect Over Time

Mean ages by strata were 2.3, 4.9, 8.1, 12.9, 23.7 and 61.0 months (Table 3). Significant effects with age (at visit) as a fixed factor were seen for IH biological elasticity, overall elasticity, net elasticity, viscoelasticity and elastic recovery ($p < 0.05$). IH difference from control with age was significant for biological elasticity, overall elasticity and net elasticity ($p < 0.05$).

There were significant group effects for IH viscoelasticity and elastic recovery difference (IH – control) ($p = 0.2$, $p < 0.001$, respectively). IH viscoelasticity was higher at 2.3 than 12.9, 23.7 and 61.0 months and higher at 4.9 and 8.1 than 61.0 months (Figure 5a). The Ur difference increased over time due to lower values for IH than controls. Differences were smaller at 2.3 versus 23.7 and 61.0 months and smaller at 4.9 and 8.1 than 12.9, 23.7 and 61.0 months (Figure 5b).

Effect of Size

There were weak but statistically significant correlations among IH volume, height, biological elasticity, net elasticity, and residual deformation. Since IHs varied considerably in size, the data were stratified into 5 groups to determine the effect on biomechanical outcomes. Mean volumes were 0.4, 1.8, 4.6, 10.1 and 26.4 mm³. Biological elasticity increased and residual deformation decreased with increasing volume, with values for 10.1 and 26.4 mm³ differing from all others ($p < 0.05$) (Figure 6, Table 4).

Histology

Biomechanical responses were measured for 11 IHs (and controls) prior to excision and paralleled the larger group for Ur/Uf, Ua/Uf, Ur/Ue, Uv/Ue, R and Ur. IHs and controls did not differ for Uf, Ua, Ue, or Uv, likely due to the small sample size. The histology results are summarized in Supplementary Table 1. Figure 7 shows representative H&E sections. Stages assessed clinically, prior to excision, were proliferating (Figure 7a), stable (Figures 7b, c) and completely involuted (Figure 7d). Figure 7a (face/temple) shows an IH with superficial and deep components characterized by back to back capillaries with minimal intervening stroma lined by plump endothelial cells mixed with pericytes. There are scattered mast cells. Occasionally, if there is epidermal ulceration, inflammatory cells may be present. Epidermal rete ridges were not observed. In contrast, the IH in figure 7b (cheek) displayed lobules of capillaries lined by flattened endothelial cells, hyalinized capillary basement membrane, and increased fibrous stroma in between and capillaries and lobules. Fat and fibrous tissue replacement demonstrated involution. Figure 7c shows an IH near the ear, excised at 23 months, with a normal, thick epidermis. The lesion was within the superficial papillary and deep reticular dermis extending into the subcutaneous layer. The vessels, arranged in lobules, showed similar involutional changes as 7b with prominent hyalinization of the capillary basement membrane and increased stroma in between the capillaries. IH morphology was confirmed with immunoexpression of CLUT-1 within the capillary endothelial cells. The IH from the chest at 76 months (Figure 7d) showed no evidence of residual vascular lesion and only mature fibroadipose tissue.

Discussion

The objectives were to quantify the biomechanical properties of IHs relative to contralateral uninvolved control sites, as a function of clinical stage, depth, size, and time (age) using suction to create mechanical stress. The 88 subjects (102 IHs) encompassed a range of disease progression. Sixty-seven females and 21 males reflected the 3:1 gender distribution (10). Thirty-four percent of IHs on the head/neck was lower than the expected 60% (4).

Infantile hemangiomas displayed greater deformation, i.e., total, elastic, residual, and lower recovery from stress than contralateral normal skin. They were less elastic and had greater viscoelastic creep (Figures 1, 2 a,b). The biomechanical properties of infantile hemangiomas differed considerably by body site for: abdomen/chest, leg, arm/shoulder, back, head and face. The elastic recovery difference (IH – control) for both leg and head sites differed from all others (Figure 3) (Table 2). The largest elastic recovery difference (versus control) was for skin from the abdomen and the smallest, i.e., most similar to normal skin, was for the head. Superficial IHs were more viscoelastic than mixed lesions. The viscous properties, i.e., viscoelasticity and viscoelastic creep, differentiated clinically assessed involuting IHs from proliferating and/or stable IHs (Figure 4).

Infantile hemangiomas were highly variable in size, as expected for our specialized clinic. The mean volume was 6.2 mm³ (median 3 mm³), the range from < 0.5 to 57 and 70% were less than 7 mm³. When analyzed by volume strata, the largest tumors had greater biological elasticity and lower residual deformation than smaller IHs (Figure 6). This suggests that size influences IH elasticity for relatively larger tumors. However, additional studies are required to confirm the influence of size in smaller IHs, i.e., less than about 7 mm³.

IH response to mechanical stress changed significantly with age and age group (time) versus control for two properties. IH viscoelasticity was highest for the youngest group which decreased significantly over time by 12.9 months. Viscoelasticity was higher for infants of 4.9 and 8.1 months compared to the oldest group (Figure 5). IH elastic recovery decreased versus control skin. Elastic recovery difference increased from smaller values at 2.3, 4.9, and 8.1 months versus larger differences at 23.7 and 61.0 months. Overall, the results provided a consistent picture of IH tissue response to stress. Elastic recovery was lower than normal and lessened over time, with involution. Biological elasticity varied with body site and size but was lower than normal skin. Over time, the viscous component, i.e., viscoelasticity, decreased.

The epidermis, fibrous collagen and elastin network in the dermis, and the hypodermis create the skin's biomechanical behavior. When measured with the 6 mm probe, changes are attributed to the dermis (24). Biological elasticity (U_r/U_f), the ability to return to initial position after deformation (25), derives from the elastic fiber network (26). Histology showed the IH features and impact on dermal structure (Figure 7, Supplementary Table 1). The tumor in Figure 7a resulted in loss of rete ridges. Tumor infiltration, e.g., capillary networks was observed in the proliferating and stable IHs (Figures 7a, b, c), resulting in disruption of the normal dermal architecture. The IH in Figure 7c was deeper, relative to those in Figures 7a and b. These figures also provide an indication of the variation in IH

characteristics, i.e., size, depth, and may account for the biomechanical response. The high residual deformities observed in this study are explained by changes over time. Specifically, as capillaries in IHs involute, there is increasing amounts of dermal fibrosis and fat replacement of normal collagen and elastin bundles. The extent of these changes is dependent on the size and depth of the lesion.

To our current knowledge, this is the first report to evaluate vascular tumors, specifically infantile hemangiomas, with mechanical suction stress methods. Consequently, comparisons to the literature are limited to other skin conditions where dermal architecture may be modified. Overall and net elasticity were higher and residual deformation lower six months after perioral resurfacing with a CO₂ laser versus dermabrasion (18). Graft seam elasticity increased after two treatments with pulsed-dye laser and compression versus compression alone (27). Skin elasticity increased after treatment of gynoid lipodystrophy (cellulite) with extracorporeal pulse activation therapy (28). Skin exposed to cold injury showed initial increases in elasticity followed by a decrease, indicating dermal damage (29). Doppler ultrasound and strain elastography have successfully characterized skin melanomas as elasticity measured this way was related to tumor vascularization(30). To date, these methods have not been used to evaluate IH elasticity.

Some specific features of this study were noteworthy, as they emphasize the utility and potential limitations of the results. The study was not controlled, with variations in the number of evaluations per subject and the intervals between measurements and necessitated classification by age to assess responses over time. Group age ranges were somewhat arbitrary but reflected times of expected IH changes. Since IH locations and treatment varied among evaluations, body site and treatment were included in the statistical model to control for them. A number of factors influenced the biomechanical response, including body site, tumor size, age, tumor depth (superficial, mixed) and treatment protocol. While there were 88 subjects and multiple evaluations, it is not possible to accurately determine how these factors interact to impact biomechanical behavior. Therefore, the findings are considered preliminary. Additional subject evaluations are required to fully establish the impact of lesion attributes on biomechanical behavior and, thereby, determine thresholds for clinical stage and disease progression. The cohort of histology subjects was small and limited by the time of excision, rather than being collected at prescribed time. Thus, it was not possible to fully relate the biomechanical properties to IH structural features from histology. Additional studies are warranted with a larger sample size to encompass IH variability, enrollment within 2-3 weeks of birth, multiple visits per subject at specific intervals, and over longer duration, e.g., 5 years, to encompass proliferation, stabilization and involution within subjects. Ideally, biomechanical properties are measured along with objective methods, such as color, three-dimensional, and dynamic thermal imaging (13). In vivo methods, such as color Doppler ultrasound and confocal microscopy, are recommended for non-invasive characterization of IH structure since standard histology is not feasible.

Nevertheless, the dynamic measurements of IH biomechanical response were well-tolerated by young subjects. The method quantified IH tissue properties relative to the subject's control skin, showed differences among specific features and differentiated involuting IHs from proliferating or stable lesions. The quantitation of biomechanical behavior at routine

clinic visits may assist clinicians in determining the rate of change and, thereby, the effectiveness of a treatment. Clinically, knowledge of when involution predominates is important for deciding whether to continue treatment. In this study, the method was not particularly effective for distinguishing proliferating from stable IHs. Further investigation is needed to discern the capabilities and limits of the method and should include evaluation of other modes of creating biomechanical stress, e.g., indentometry, an instrumental technique that is more similar to palpation than suction methods (31).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Schematic of Cutometer Mode 1 Illustrating Measured Parameters

Stress versus time relationships for mechanical property measurements are as follows:

Biological elasticity (U_r/U_f), overall elasticity (U_a/U_f), net elasticity (U_r/U_e), viscoelasticity (U_v/U_e), elastic recovery (U_r), residual deformation (R), total recovery (U_a), viscoelastic creep (U_v), elastic deformation (U_e), and total deformation (U_f)

Figure 2 a, b. Biomechanical Properties of Infantile Hemangiomas and Control Sites

Biological elasticity (Ur/Uf), overall elasticity (Ua/Uf), net elasticity (Ur/Ue), total recovery (Ua) and elastic recovery (Ur) were lower for IH versus controls ($p < 0.001$) (Figure a,b).

Total deformation (Uf), elastic deformation (Ue), viscoelastic creep (Uv) and residual deformation (R) were higher for IHs versus controls ($p < 0.001$) (Figure a). * Indicates significant difference for IH versus control.

Figure 3 a, b. Effect of Body Site

Elastic recovery difference was higher for abdomen and leg and higher for the head than all others (Figure a). IH net elasticity for the head was lower than all other sites; higher for leg versus arm, head and face; and higher for abdomen versus arm and head ($p < 0.05$) (Figure b). * Indicates significant difference from all other sites. # Indicates significant differences versus arm, head and face. ‡ Indicates significant difference for abdomen versus arm and head.

Figure 4. Effect of Clinically Assessed Stage

Viscoelasticity (Uv/Ue) was lower for involuting compared to proliferating and stable IHs ($p < 0.001$). Viscoelastic creep (Uv) was lower for involuting versus stable IHs ($p = 0.04$). *

Indicates significant different from proliferating and stable IHs. # Indicates significant difference from stable IHs.

Figure 5 a,b. Effect Over Time

IH viscoelasticity was higher at 2.3 compared to 12.9, 23.7 and 61.0 months and higher at 4.9 and 8.1 than 61.0 months (Figure a). The Ur difference increased over time due to lower values for IH than control skin. Differences were smaller at 2.3 versus 23.7 and 61.0 months and smaller at 4.9 and 8.1 versus 12.9, 23.7 and 61.0 months (Figure b).

Figure 6. Effect of IH Size

Biological elasticity increased and residual deformation decreased with increasing volume, with values for the 10.1 and 26.4 mm³ strata differing from all others ($p < 0.05$)

Figure 7 a, b, c, d. Representative Histology from Excised Infantile Hemangiomas

Four infantile hemangiomas and the respective histology (H&E stain) are shown. Clinically assessed stages (before excision) were proliferating (Figure a), stable (Figures b, c) and involuting (Figure d). The face/temple IH in Figure a had superficial and deep components, sheets of capillaries lined by plump endothelial cells mixed with pericytes with little intervening stroma. The basement membrane of the capillaries is thin. Scattered mast cells are present. Rete ridges were not observed in the epidermis. The cheek IH in Figure b showed capillaries in multiple lobules with central vessels. These vessels are lined by

flattened endothelial cells and have increased stroma in between the capillaries. Fat and fibrosis tissue replacement indicate involution. The IH in Figure c, excised from near the ear at 23 months, showed a normal, thick epidermis. The lesion was within the superficial and deeper dermis extending into the subcutaneous layer and had similar involutional changes as Figure b. The IH in Figure d from the chest at 76 months showed no evidence of a vascular lesion and only mature fibroadipose tissue.

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Table 1

Infantile Hemangiomas - Anatomical Locations of and Distribution

Location	Number Evaluations (%)	Number Sites (%)
Abdomen/Chest	36 (18.5)	23 (22.5)
Leg/hip	18 (9.2)	9 (8.8)
Arm/shoulder	39 (20.0)	21 (20.6)
Back	25 (12.8)	14 (13.7)
Head	17 (8.7)	8 (7.8)
Face	60 (30.8)	27 (26.5)
Total	195	102

Table 2**Biomechanical Property Statistics by Body Site^{*}**

As Difference (IH – Control)		
	F statistic, p value	Group Comparisons
Total deformation (Uf)	2.37, p = 0.041	F –s- Ab, AS, H
Residual deformation (R)	2.66, p = 0.024	F –s- Ab, AS, H
Viscoelasticity (Uv/Ue)	2.1, p = 0.065	-----
Biological Elasticity (Ur/Uf)	3.2, p = 0.008	Ab –s- AS, B, H, F
Total recovery (Ua)	2.88, p = 0.016	Ab –s- AS, F B –s- F
Elastic deformation (Ue)	2.56, p = 0.029	AS –s- Ab, L, F H –s- Ab
Elastic recovery (Ur)	21.74, p < 0.001	Ab –s- L, AS, B, H, F L –s- Ab, AS, B, H, F H –s- Ab, L, AS, B, F
Hemangioma Values^{**}		
Overall elasticity (Ua/Uf)	2.95, p = 0.014	H –s- Ab, L, AS, B, F
Net elasticity (Ur/Ue)	4.18, p = 0.001	Ab –s- AS, H L –s- AS, H, F AS –s- Ab, L, H H –s- Ab, L, AS, B, F
Viscoelasticity (Uv/Ue)	4.19, p = 0.001	F –s- Ab, L, B, H AS –s- L, B
Biological Elasticity (Ur/Uf)	3.13, p = 0.01	H-s- Ab, L, AS, B, F L-s- AS
Elastic deformation (Ue)	2.38, p = 0.04	Ab-s- L, F L-s- Ab, AS AS –s- L, B, F
Viscoelastic creep (Uv)	3.28, p = 0.007	F –s- Ab, L, AS, B, H
Elastic recovery (Ur)	1.98, p = 0.083	-----

* Ab = abdomen/chest, L = leg/ankle, AS = arm/shoulder, B = back, H = head, F = face

** Control site was a covariate in the analysis

Table 3

Demographic Characteristics for Age Groups

Group	N	Age at Evaluation Months mean $\pm$ SD	Range
1	20	2.3 $\pm$ 0.5	1.3 – 3.0
2	64	4.9 $\pm$ 1.0	3.0 – 6.8
3	38	8.1 $\pm$ 0.8	7.0 – 9.9
4	37	12.9 $\pm$ 2.3	10.1 – 17.3
5	22	23.7 $\pm$ 4.5	19.9 – 34.8
6	14	61.0 $\pm$ 29.4	36.4 – 144.4
Total	195		

Table 4

Effect of IH Size on Biomechanical Properties

Hemangioma Values	F statistic, p value	Group Comparisons
Biological Elasticity (Ur/Uf)	5.43, $p < 0.001$	Mean 10.1 and 26.4 –s- all
Overall elasticity (Ua/Uf)	4.86, $p = 0.001$	Mean 10.1 and 26.4 –s- all
Net elasticity (Ur/Ue)	4.51, $p = 0.002$	Mean 10.1 and 26.4 –s- all
Viscoelasticity (Uv/Ue)	2.75, $p = 0.03$	26.4 –s- all 10.1 –s- 0.4, 1.8
Elastic recovery (Ur)	4.03, $p = 0.002$	26.4 –s- all 10.1 –s- 0.4, 1.8
Residual deformation (R)	3.18, $p = 0.015$	26.4 –s- all 10.1 –s- 0.4, 1.8
Total recovery (Ua)	2.68, $p = 0.033$	26.4 –s- all 10.1 –s- 0.4
Viscoelastic creep (Uv)	3.54, $p = 0.008$	26.4 –s- all 10.1 –s- 0.4, 1.8