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Microstructural and mechanical characterization of human tissue at and adjacent to pressure ulcers

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Abstract—This investigation evaluated the microstructural and mechanical properties of human skin at and adjacent to pressure ulcers (PUs). Healthy breast and leg tissue served as control tissue. The tissue was characterized through uniaxial tensile testing and histomorphometric analysis. The PU tissue had significantly fewer straight and wavy fibers, but the fibers present were significantly wider and longer than those found in the healthy control tissue. PU ulcer tissue tested in tension had significantly lower strains at peak stress, versus the control breast tissue. Tissue at and adjacent to PUs has undergone significant adaptation or remodeling, as a result of the pressure sustained by the tissue.

KEY words: *collagen, decubitus ulcer, microstructure, pressure, pressure ulcer, skin, strain, stress.*

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INTRODUCTION

This research evaluated the microstructural and mechanical effects of pressure ulcers (PUs) on human tissue. Results from the microstructural and mechanical analysis of tissue at and adjacent to PUs were compared with results from healthy tissue.

Chronic disease and disability may result in abnormal loading of tissues, due to paralysis, decreased sensation, and prolonged bedrest or sitting (1). The abnormal mechanical loads, which the skin and tissues must bear result in tissue breakdowns. Sustained pressure over a period of time leads to cellular necrosis and tissue breakdown (1–10). The skin ulcerations, which occur as a result of this tissue damage, are known as decubitus ulcers, or PUs.

The prevalence of PUs has been reported to be as high as 11 percent of the hospitalized population and 20 percent of the nursing home population (11). The cost associated with the treatment of these wounds is staggering and is estimated to exceed seven billion dollars a year (12). Thus, there has been a sharp focus on prevention of PU formation. In particular, interface pressures have become increasingly scrutinized as the effects of pressure on tissue have become evident (13–22).

The results of pressure differ between individuals. Some of the individuals will develop PUs, while others will

not, and the severity of the ulcers varies (23). Pressure or other mechanical loads do cause alteration or adaptation of tissues (1). The adaptation of tissue to pressure may be invaluable in preventing PUs or tissue breakdown.

In normal skin, collagen remodeling occurs as a response to mechanical stresses and during wound healing (1,24,25). Craig et al. (24) have found that collagen fibril size distributions relate to the mechanical role of skin. Skin that functions in locomotory or postural functions has larger diameters of fibrils versus skin, which does not have these functions. Michna et al. (26) reported increased collagen diameter in tendons and ligaments with increased exercise.

Previously we have evaluated the mechanical and microstructural effects of pressure on human skin in vitro (27,28,29). The pressures evaluated were based on common interfacial pressures at the heel of subjects on pressure relief systems. Realignment of the collagen bundles within the tissue occurred, but directionality varied depending on whether the pressure was continuous or cyclic. The mechanical results showed a decrease in the tissue's stiffness after pressure was applied. Tissue subjected to static pressure had a greater reduction in stiffness than tissue subjected to dynamic pressure. Thus, pressure application did alter the microstructural and mechanical properties of the tissue.

Based on this work, we hypothesize that tissue at and adjacent to PUs will be microstructurally and mechanically altered, as compared to healthy tissue.

METHODS

Tissue surgically debrided at and adjacent to PUs was used for this study. The tissue was placed in 10 percent buffered formalin postsurgical debridement. The tissue samples were obtained from 17 male and female patients with wounds requiring debridement. Three of the 17 decubitus ulcer samples were omitted from the study because they were not true PUs, but were, rather, venous ulcers or other types of wounds. Five samples were omitted from the sample due to size limitations, which prevented their being tensile tested. The tissue samples used were all from Caucasian female patients with an age range of 66–102 years and average age of 82 years, a height range of 149.86–178 cm with an average of 161.48 cm, and a weight range of 37.92–201.90 kg with an average of 72.41 kg. Often, samples from different sites of the same patient were obtained. The most common sites of decubitus ulcer formation were hips, sacrum, and heels. The ulcers ranged in stages with nine samples of Stage IV, two stage III, and two stage II. Staging was performed using the NPUAP staging system. Information about patients' health history, diagnostic, and/or laboratory tests taken on or close to the date of admission, as well as wound stage, treatment, and bed surface used up until the day of debridement, were all recorded into a main database. Healthy breast tissue from a Caucasian female age 76 and tissue from the lower leg of an adult male were used for the study as non-pressure ulcer tissue controls.

The TR500 mechanical tester (Columbia Laboratories, Inc., Buffalo, NY) was used for testing the mechanical tensile strength of the tissue. The load frame of the TR500 consists of a stationary lower grip, and an upper grip controlled by a 486-PC. A 25-pound load cell was used to test the tissue for all uniaxial tensile experiments. Each tissue sample was cut by using a "dog bone" shaped mold with the following dimensions: ASTM D-638 type V, width=3.18 mm and length=9.53 mm. Once the dog bone cut was made, the outer edges of the tissue were placed in a separate specimen jar with 10 percent buffered formalin and labeled as the controls. The dog bone shaped piece was mechanically tested and was considered the experimental sample (**Figure 1**).

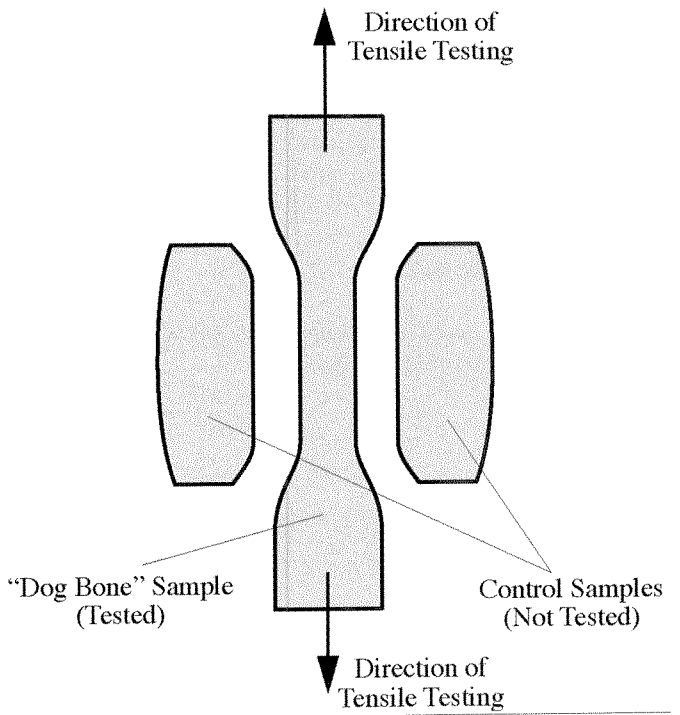

Figure 1.
Dog bone tensile test sample.

The ends of the dog bone were placed in the upper and lower grips, with the center of the shaft being the area of tensile mechanical testing. Dog bone shaft thickness and width measurements were then taken before any loads were applied. A preload force of 40 grams was applied to each experimental tissue sample prior to the experimental run. Once the preload force ceased, a length measurement was taken from between the bottom of the upper grip and the top of the lower grip. At this point the tissue was ready for the experimental run. The upper grip pulled on the tissue at a rate of 20 mm/min. The tissue was tested to failure, and a corresponding stress/strain graph was created from the computer-acquired data from each run. Following testing, the sample was placed in 10 percent buffered formalin.

The tissue was processed in alcohols from 70 percent to 100 percent, then cleared in xylene before it was embedded in paraffin. The tissue samples were serially sectioned at 5 microns. Slides 1, 4, 7, and so on were stained using Hematoxylin and Eosin; 2, 5, 8 with Masson's Trichrome, and 3, 6, 9 with Verhoeff's elastin stain. The sections stained with Masson's were used for morphometric analysis because of the resolution of fibrous components obtained with the stain. The other stains were used for comparison if necessary and to clarify tissue structures.

Morphometric analysis began with the use of the Olympus BX60 photomicroscopy system and the Hitachi KP-D550, 1/2inch CCD color digital camera, with a frame grabber which captured the image and input it into the computer, a CPU Intel Pentium Pro II Max computer with LX Chip set AGP 333 MHz, 64 MB EDO RAM and 6.4 GB HD. Image-Pro Plus version 3.0, a totally modular and expandable image analysis application, was used to analyze the image with the use of a tracing system. Both the control and experimental samples' images were analyzed at a magnification of 10×.

For each tissue sample the slide was adjusted such that the epithelial layer was positioned at the top of the computer screen. Two fields were selected for each sample. Field 1 consisted of a more superficial dermal layer and Field 2 was the adjacent deeper dermal layer. The field shots were captured using the photomicroscopy and image analysis system previously described. These fields were stored as computer files, which allowed the color intensity to be adjusted in order to enhance the image, if necessary, for analysis. This adjustment was made based on personal preference and to allow the operator the greatest contrast for the necessary measurements.

Although automatic tracing features were part of the software, all tracings were done manually to avoid any computer-generated errors due to similar color intensities between features. Once the area of interest was traced, the resultant area value, expressed in terms of 10× spatial calibration or microns, was displayed in a data sheet. Fiber bundle areas were traced, as were individual fibers and blood vessels. Any one area of fibrous tissue could consist of a single fiber, a single fiber bundle, or a group of fiber bundles running in the same orientation. Fibrous tissue areas were calculated based on total fiber bundle area minus any spaces found within the fibrous tissue. Any blood vessels present in the fibrous tissue were also subtracted from the fibrous tissue areas. Blood vessel areas were calculated based on the outer vessel wall. Thus, the lumen was included in the area calculation.

Angular orientation of each fiber bundle was also measured. A horizontal X-axis was drawn, with the vertex of the angle being on the right side. The remaining vector was aligned with the orientation of the fibers within the bundle or bundles. The angles of these orientations were measured between the range of 0 to 180°, always keeping the vector that was aligned with the fiber bundle above the X-axis. The fiber bundles, with their corresponding total area measurement, were sorted by angular measurement from lowest to highest. The bundle areas were then grouped into the following angular ranges: 165°–0°–15°; 16°–75°; 76°–90°–105°; 106°–164°; and cross-sectional. The angle range 165°–0°–15° represents the fibers including and within the horizontal orientation. Left and right oblique fiber bundles are included in the ranges 16°–75° and 106°–164°. The fibers including and within the vertical orientation are in the 76°–90°–105°range. Fiber bundles running perpendicular to the field plane were labeled as cross-sectional. A final total fiber area was then summed for each of these ranges.

Length and width measurements of fibers were made. Because bundles differed dramatically between straight and wavy, they were subjectively grouped as wavy if two or more bends were present in the fiber. The wavy length measurements followed the bends in the fiber bundles.

RESULTS

The results were analyzed according to five different groups: PU tissue non-tested, PU tissue tested, leg control tissue, breast control tissue, and breast tested tissue. The

groups of tissue were subjected to different types of analyses, depending on their categories. Patient database information, mechanical testing data, and histomorphometric data were the categories of analysis.

Patient Database Results

The patient database contained headings for ulcer site, debridement date, sex, race, height, weight, age, smoker, diabetic, cardiovascular disease, cancer, chemotherapy, radiation, connective tissue disease, neuromuscular complications, glucose, creatin, BUN, CO_2, cholesterol, albumin, protein, WBC, RBC, hemoglobin, platelet, prothrombin, whirlpool, topicals applied, packed wound, culture growth, support surface, and stage of wound. There were no consistent associations with fiber direction, fiber area, blood vessel area, or fiber dimensions with the headings found in the patient database. There were no significant correlations between peak tensile strength or strain associated with peak tensile strength.

Mechanical Testing Results

The stress/strain graphs associated with the tensile testing were extremely variable (see **Table 1**).

Table 1.
Mean peak stress (psi) and associated strain for tested pressure ulcer and breast tissue.

Tissue Group	Peak Stress	Strain
Pressure Ulcer (n=13)	464.3±576.7	32.6±16.5
Breast (n=2)	197.1±72.0	61.7±17.3

In order to analyze these data, the peak stress values, which ranged from 9.19–2050.91 psi, and the strain (4.36–69.53 percent) associated with the stress, were used. To examine relationships among mechanical data (peak stress and associated strain) and fiber dimension metrics and directionality, multiple correlations were used. The peak stress was not normally distributed, so Spearman's rank correlation was used to test for association between the peak stress and all of the other variables. There were no consistent associations with fiber direction and either fiber dimensions or peak stress in PU tissue, but peak stress values were significantly correlated with several fiber dimensions. In PU tissue, peak stress was negatively correlated with the length of the wavy fibers ($r=-0.490$, $p=0.0177$). Strain was negatively correlated with both length ($r=-0.462$, $p=0.023$) and width ($r=-0.431$, $p=-0.031$) (see **Table 2**).

Table 2.
Correlations found in pressure ulcer tissue between mechanical properties and fiber dimensions.

Fiber Dimension	Peak Stress	Peak Strain
Wavy Length	Negative Correlation	No Correlation
Straight Length	No Correlation	Negative Correlation
Straight Width	No Correlation	Negative Correlation

To analyze the relationships among peak stress measurements and tissue-specific dimensions, nonparametric Spearman's rank correlation was used. PU tissue from the hip had a significant negative relationship between peak stress and length of wavy bundles ($rs=-0.719$, $p<0.05$, $n=9$). Sacral fiber width and peak stress were positively associated ($rs=0.914$, $p<0.05$, $n=6$) and the length of these fibers was positively associated with strain ($rs=0.971$, $p<0.05$, $n=6$).

Fiber dimensions are shown for both groups based on fields 1 and 2 (n=26 for PU tissue and n=4 for breast tissue) in **Table 3**.

Table 3.
Fiber dimensions (μm) for tested pressure ulcer and breast tissue

Tissue Group	Straight Length	Straight Width	Wavy Length	Wavy Width
Pressure Ulcer (n=13)	50.6±21.3	16.3±5.4	140.2±45.3	17.4±8.4
Breast (n=2)	35.9±4.4	12.1±2.5	90.3±7.3	10.5±2.2

Histomorphometric Results

The non-tested PU samples appeared different from the healthy leg and breast tissue, based on the distribution and size of the fibers. **Figures 2** and **3** are typical fields seen for these groups. Note the shorter and thinner fibers seen in the healthy leg tissue versus the thick long bands of fibers seen in the non-tested PU tissue. Both the breast and leg tissue appeared similar.

To determine whether fibers in tested tissue were altered during the tensile testing, tested tissue was compared with untested tissue from the same pressure sore. A paired t-test was conducted for each of four directions

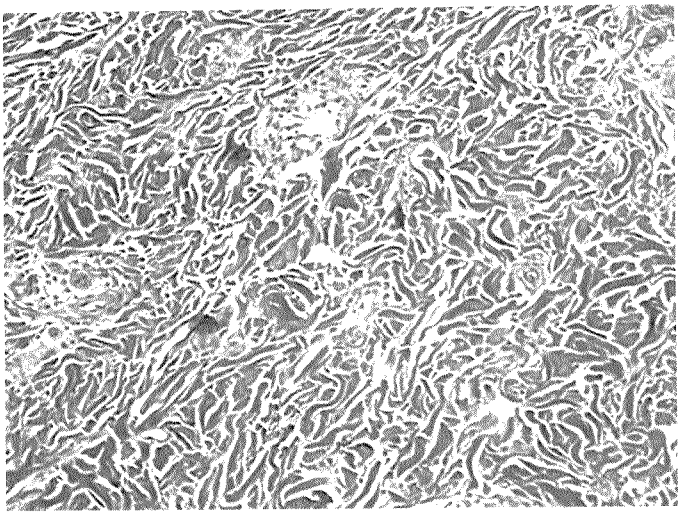

Figure 2.
Leg control tissue.

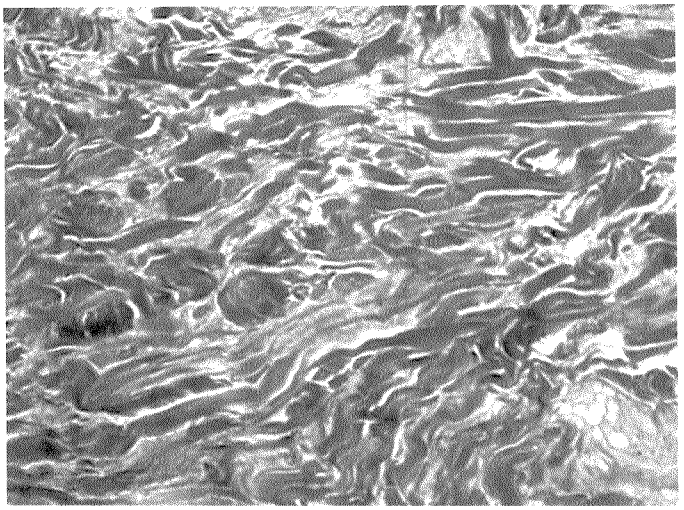

Figure 3.
Non-tested pressure ulcer tissue.

(vertical, horizontal, diagonal, or cross-sectional) using an adjusted alpha for multiple tests. Proportion of fibers in a given direction was arcsine square root transformed prior to analysis. Fiber direction did not differ significantly between non-tested and tested PU tissue ($p>0.1$ for all comparisons). To test whether fiber dimensions varied between tested and non-tested samples from the same PU, paired t-tests were conducted using lengths and widths of straight and wavy fibers. Regardless of tissue depth (field), fiber dimensions did not vary between non-tested and tested PU tissue ($p>0.15$ for all comparisons) (see **Table 4**). Paired t-tests were used to distinguish differences between fields (tissue depth) in fiber directionality. Tissue depth or fields did not differ in their fiber directionality ($p>0.1$ for all comparisons).

Table 4.
Fiber directions and dimensions in tested versus untested pressure ulcer tissue.

	Tested vs. Untested Pressure Ulcer
Direction	Did not differ significantly ($p>0.1$)
Dimensions	Did not differ significantly ($p>0.15$)

To test the hypothesis that PU tissue was histomorphometrically different from healthy breast or leg tissue, two sample t-tests were used to compare mean proportion of fibers in each of the directions as well as mean fiber dimensions between healthy tissue and PU tissue. Proportions of fibers in a given direction were arcsine square root transformed prior to analysis. Although fiber directionality did not vary between non-tested PU tissue and healthy leg or breast tissue ($p>0.28$), fiber dimensions were significantly different (see **Tables 5** and **6**).

Table 5.
Fiber directions and dimensions in nontested pressure ulcer tissue versus healthy leg or breast tissue.

	Healthy leg or breast vs. Nontested Pressure Ulcer
Direction	Did not differ significantly ($p>0.28$)
Dimensions	Did differ significantly

Table 6.
Fiber directionality for nontested and tested pressure ulcer tissue.

	Fiber Directionality (% of Total)			
Tissue Group	**Horiz**	**Vert**	**Diag**	**Cross**
Nontested Pressure Ulcer	16.8	11.5	71.7	0.0
Healthy Leg and Breast	18.7	11.9	69.4	0.0

Horiz=horizontal, vert=vertical; diag=diagonal; cross=cross-sectional.

Length and width of both straight and wavy fibers varied significantly ($p=0.0001$ in all cases). Leg control tissue had significantly shorter straight and wavy fibers than the non-tested PU tissue ($p>0.0001$). Breast control tissue also had significantly shorter straight and wavy fibers than the non-tested PU tissue ($p>0.0001$). Non-tested PU tissue had wider straight and wavy fibers than

both leg control tissue and breast control tissue ($p>0.0001$) (see **Table 7**). Breast control tissue had significantly longer straight and wavy fibers than leg control tissue ($p>0.0001$), but the width of wavy fibers was significantly less for breast control tissue than leg control tissue. The width of the straight fibers did not vary significantly between breast control and leg control tissue. The fiber dimensions for both the non-tested PU tissue and the healthy breast or leg tissue are shown in **Table 8.**

Table 7.
Fiber directions and dimensions in nontested pressure ulcer tissue versus healthy nontested leg or breast tissue.

Dimensions	Healthy leg or breast vs. Nontested Pressure Ulcer
Length	Shorter fibers in leg and breast tissue
Width	Thinner fibers in leg and breast tissue

Table 8.
Fiber dimensions (μm) for nontested and tested pressure ulcer tissue.

	Straight Fibers		Wavy Fibers	
Tissue Group	**Length**	**Width**	**Length**	**Width**
Nontested Pressure Ulcer	57.74	18.75	138.87	19.36
Healthy Leg and Breast	55.57	18.06	127.29	18.14

The number of straight fibers and the number of wavy fibers was significantly greater for both the leg and the breast control tissue, than for the tested and non-tested PU tissue. The number of straight fibers in the non-tested PU tissue was not significantly different from the number in tested PU tissue. This was also true for wavy fibers. The number of wavy and straight fibers was significantly greater in both the breast and leg tissue than in the tested and non-tested PU tissue ($p=0.0001$). The number of straight and wavy fibers in the breast control tissue was not significantly different than in the leg control tissue ($p=0.001$; see **Table 9**).

Table 9.
Mean number of straight and wavy fibers in tissue groups.

Tissue Group	Straight	Wavy
Nontested Pressure Ulcer	63.2±43.4	63.9±40.6
Tested Pressure Ulcer	64.5±46.9	66.5±43.6
Control Breast	213.0±42.3	118.5±23.9
Control Leg	184.5±42.3	130.5±25.0

DISCUSSION

The patient database results produced no consistent associations with fiber direction, fiber area, blood vessel area, fiber dimension, or mechanical properties. Over the course of the study we collected samples from 17 patients in the 413-bed hospital. The tissue collected was from those ulcers or wounds requiring debridement only. The samples varied tremendously in patient information. The mean age of the patients from whom the tissue was collected was 82 years. By this point in a person's life, significant differences exist between individuals, based on dietary, exercise, and health habits. Taking these factors into consideration along with the reason for admittance to the hospital, general health, course of treatment for other problems, the variations between individuals is enormous. Furthermore, the inclusion of support surface as a category is very complicated, because a patient is probably on a different support surface in their home or nursing home prior to admission. The differences between these surfaces are tremendous, and no consistent associations between surface and microstructural or mechanical properties was present.

The large ranges seen in the mechanical data were unexpected. Previous studies with healthy human skin collected from newborn males and with other tissue types showed much narrower ranges (28,30). One explanation for this great variability is the differences in tissue collected from around a pressure sore. During debridement tissue from the margin of the wound was collected, but due to tunneling and severity of the ulcer, the tissue varied in thickness and layers present. Non-tested and tested PU tissue did not have significant differences in fiber direction or dimensions. The tensile testing had no significant histomorphometric effect on the PU tissue.

There is such a large range of peak stress values for PU tissue, that the standard deviation is greater than the mean. Although the mean of the tested breast tissue is much lower, there is no significance to this difference in mean values because of the large PU tissue standard deviation. The strain values are significantly greater for the breast tissue versus the PU tissue. The PU tissue has been altered such that the tissue does not extend as much under load as the breast tissue. The mechanical properties of collagen are correlated with fiber dimension. Dimensions of fibers increase with increased loading (13,14,31). PU tissue did have increased fiber width as a result of the remodeling due to the abnormal loading sustained by the tissue.

There was no consistent association with fiber direction and either fiber dimension or peak stress, but peak stress was significantly correlated with several fiber dimensions. In tested PU tissue, peak stress was negatively correlated with the length of wavy fibers, and strain was negatively correlated with length and width of straight fibers. As the load is increased in tension, the collagen bundles straighten and resist further extension. As the fibers change during stretching of the tissue, the waviness of the collagen fibers is reduced. The fibers begin to straighten and the stress required to further strain the tissue increases. The decrease in the length of wavy fibers is indicative of longer fibers straightening to resist the load (32–34). Several investigators have demonstrated that, as collagen fibers align in the direction of the force, there is an increased resistance to extension of the tissue in that direction (32–34).

Specific sites of PU tissue had different relationships with peak stress measurements. PU tissue from the hip had a significant negative relationship between peak stress and length of wavy fibers. Sacral PU tissue peak stress was positively associated with straight fiber width, and strain was positively associated with the length of these fibers. The negative correlation with peak stress and wavy fiber length at the hip in tested PU tissue is indicative of fibers straightening as a load is applied, as previously reported by (32–34). Tested PU tissue from the sacrum had peak stress positively associated with increased fiber width. Previously, investigators have reported an increase in fiber diameter based on usage (14,35). The positive association between strain and fiber length in the sacral site has been previously seen in skin in initial extension of the collagen network as the fibers unfold and lengthen (33).

Tissue fiber directionality and dimensions were significantly different between fields. For each tissue sample, the 1st field was chosen such that the epithelial layer was at the top of the screen. The 2nd field was the adjacent deeper dermal layer. Thus, the tissues being compared were from superficial and deeper dermal layers in each case. The analysis sought to compare similar tissue for each field. Tissue depth did not affect the histomorphometric results. The breast and leg control tissues were not different in either number or width of straight or wavy fibers, but breast had longer straight and wavy fibers than leg. Breast control tissue had significantly longer straight and wavy fibers than leg control tissue, but the width of wavy fibers was significantly less for breast control tissue than leg control tissue. The width of the straight fibers did not vary significantly between breast control and leg control tissue. Thus, the control tissues were very similar, although they were from two different sites on the body. Since our PU samples were from multiple sites on the body, it was of great importance that our control tissues be comparable between sites. The increased length in fibers in the breast may be a function of the 36DD breast size, which weighed 560 grams at reduction, straightening the fibers. The weight of this tissue would contribute to increased stress, unlike the leg tissue.

Ideally, healthy tissue from identical sites from a similar population would be used for the control tissue. Initially we prepared tissue from gross anatomy academic cadavers, but we found the histological results were of poor quality. It may be that the embalming process destroys many of the fibrous tissue components we were interested in evaluating. It was not possible for us to obtain tissue from cadavers prior to embalming. The ideal control would be the patient's own tissue as a positive control, but it is not possible to enlarge a wound to that degree or to create a new wound. There are age-related changes in tissue, and it is difficult to obtain age-matched tissue for each patient. The tissue of the 76-year-old female was a good reference tissue, because by age 70 the age-related changes have occurred in the skin. The skin has thinned and the collagen/elastin bonds have changed generally by the 70's, but these changes may not be unequivocally the same.

Both breast and leg tissue were used to represent a locomotive, primarily muscle tissue, versus a tissue with a large glandular component in the reticular dermis and an increased concentration of fat. Breast tissue is very different from a locomotive tissue and comparison of both types of tissue to PU tissue was used to help elucidate the morphological changes present in the tissue.

The specific fibers being compared were from similar anatomic tissues, as well as different anatomical tissues. PU tissue was significantly different from leg or breast tissue, based on fiber dimensions, but not based on fiber directionality or proportions. Ultimately, the leg and breast tissue were very similar in the morphemetric properties being measured for this study. The number of straight fibers and the number of wavy fibers was significantly greater for both the leg and the breast control tissue than for the tested and non-tested PU tissue. The number of straight fibers in the non-tested PU tissue was not significantly different from the number in tested PU tissue. This was also true for wavy fibers. The number of wavy and straight fibers was significantly greater in both the breast and leg tissue than in the tested and non-tested PU tissue. The number of straight and wavy fibers in the breast control tissue was not significantly different than

in the leg control tissue. Length and width of both straight and wavy fibers varied significantly. Leg control tissue had significantly shorter straight and wavy fibers than the non-tested PU tissue. Breast control tissue also had significantly shorter straight and wavy fibers than the non-tested PU tissue. Non-tested PU tissue had wider straight and wavy fibers than both leg control tissue and breast control tissue.

We first evaluated fiber directionality and proportions because of our previous findings, which showed specific directional changes in the fibrous tissues (17,19). Our previous work, as well as that of other investigators, sought to examine the changes present in the tissue microstructure after the initial loading of tissue and damage initiation. The tissue examined in this study had endured pressure and abnormal loads for extended periods of time because of the patient's health complications. Stage IV ulcers were the most common type in our study. The tissue microstructure had been altered in the PU tissue examined in this study, as compared to the control tissue. As the tissue adapted to the abnormal loading, the fiber number and dimensions were altered compared to the control tissue. Other investigators have reported adaptation of tissue to mechanical stress in animal models of wound initiation (1,36). This study sought to examine the adaptations present in the tissue long after the wound was formed. Moore et al. (25) examined the ultrastructure of dermis in breast tissue and PUs, and he reported extensive remodeling at the surface, but noted bundles of thick fibers at the outer margin of the ulcer and finer fibrils present into the granulation edge. Changes in the rete peg structure were also reported. These changes were present in the ultrastructure of the tissue examined. Our analysis of the microstructure of these two types of tissue supported their findings of thick fibers in the PU tissue.

CONCLUSION

Our results support our hypothesis that tissue at or adjacent to PUs is microstructurally and mechanically different from healthy tissue.

The PU tissue has undergone significant microstructural adaptation or remodeling, as evidenced by the decreased number of wavy and straight fibers. The straight and wavy fibers present were longer and wider than those found in the leg and breast control tissue. Also, PU tissue tested in tension had significantly lower strains at peak stress, versus the control breast tissue. There were microstructural changes in the tissue at PUs, and these long-term changes were so severe that tensile testing did not further alter the damaged tissue microstructure.

This work provides an important view into the microstructural changes present in tissue with a long-term PU. These changes are of great importance in the design and evaluation of support surfaces, but also offer a clearer view of what can be seen when we have a window into the tissue. Ultrasound or other technology may allow a view beneath the epidermis, but without an idea of the microstructure of healthy vs. non-healthy tissue, this view cannot be used as a diagnostic tool.

Most research has evaluated the initial adaptation of microstructural changes seen in the tissue. This research examined the opposite end of the spectrum, the long-term stage IV PU. A wealth of information exists between these two ends of the wound process, and future studies should seek to elucidate the changes present along the range of wound formation to increasing severity.

The precursor to PU formation may be microstructural alignment and corresponding mechanical changes in the tissue response to the pressure conditions on the tissue. Prevention of PUs might be more successful if the earliest pressure-induced microstructural changes or adaptations in the tissue can be identified.

Future studies will seek to quantify the matrix metalloproteinases, serine proteases, cytokines, fibrinogen, and type of collagen present. Also, the period between wound formation and long-term chronic wound will be examined.

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REFERENCES

1. Sanders JE, Goldstein BS, Leotta DF. Skin response to mechanical stress: adaptation rather than breakdown—A review of the literature. J Rehabil Res Dev 1995;32(3):214–26.
2. Bader DL, Barnhill RL. Effect of externally applied skin surface forces on vasculature. Arch Phys Med Rehabil 1986;67:807–11.

3. Krouskop TA, Reddy NP, Spencer WA, Secor JW. Mechanisms of decubitus ulcer formation—an hypothesis. Med Hypotheses 1978;4:37–9.
4. Krouskop TA. A synthesis of the factors that contribute to pressure sore formation. Med Hypotheses 1983;11:255–67.
5. Daniel RK, Priest DL, Wheatley DC. Etiologic factors in pressure sores: an experimental model. Arch Phys Med Rehabil 1981;62:492–8.
6. Reddy NP, Cochran GVB, Krouskop TA. Technical note: interstitial fluid flow as a factor in decubtius ulcer formation. J Biomech 1981;14(12):879–81.
7. Reuler JB, Cooney TG. The pressure sore: pathophysiology and principles of management. Ann Int Med 1981;94:661–6.
8. Rodriguez GP, Murphy KP. Current trends in pressure ulcer research. Crit Rev Phys Rehabil Med 8(1&2):1–18 (1996).
9. Rudd TN. The pathogenesis of decubitus ulcers. J Am Ger Soc 1962;10:48–53.
10. Yarkony GM. Pressure ulcers: A review. Arch of Phy Med Rehab 1994;75:908–17.
11. Sanders SL. Pressure ulcers, Part I: prevention strategies. J Am Acad Nur Prac 1992;4(2):63–70.
12. Maklebust J, Mondoux L, Sieggreen M. Pressure relief characteristics of various support surfaces used in the prevention and treatment of pressure ulcers. J Enterost Ther 1986;13:85–9.
13. Barbenel JC, Sockalingham S. Device for measuring soft tissue interface pressures. J Biomed Eng 1990;12:519–22.
14. Berjian RA, Douglass HO, Holyoke ED, Goodwin PM, Priore RL. Skin pressure on various mattress surfaces in cancer patients. Am J Phys Med 1983;62:217–26.
15. Goldstone LA, Norris M, O'Reilly M, White J. A clinical trial of bead bed system for the prevention of pressure sores in elderly orthopaedic patients. J Adv Nurs 1982;7:545–8.
16. Barnett RI, Shelton FE. Measurement of support surface efficacy: pressure. Adv Wound Care 1997;10(7): 21–9.
17. Burman PMS. Using pressure measurements to evaluate different technologies. Decubitus 1993;6(3):38–42.
18. Daechsel D, Conine TA. Special mattresses: effectiveness in preventing decubitus ulcers in chronic neurologic patients. Arch Phys Med Rehab 1985;66:246–8.
19. Hasty JH, Krasner D, Kennedy KL. A new tool for evaluating patient support surfaces, Part I: a guideline for making practice decisions. Ostomy/Wound Man 1991;36:51–9.
20. Hofman A, Geelkerken RH, Wille J, Hamming JJ, Hermans J, Breslau PJ. Pressure sores and pressure-decreasing mattresses: controlled clinical trial. Lancet 1994;343:568–71.
21. Maklebust J, Mondoux L, Sieggreen M. Pressure relief characteristics of various support surfaces used in prevention and treatment of pressure ulcers. J Enterost Ther 1986;13:85–9.
22. Shelton F, Barnett R, Meyer E. Full body interface pressure testing as a method for performance evaluation of clinical support surfaces. J Appl Ergonom, May 1997:1–20.
23. Meijer JH, Germs PH, Schneider H, Ribbe MW. Susceptibility to decubitus ulcer formation. Arch Phys Med Rehabil 1994;75:318–23.
24. Craig AS, Eikenberry EF, Parry DAD. Ultrastructural organization of skin: classification on the basis of mechanical role. Conn Tiss Res 1987;16:213–23.
25. Moore JC, Ray AK, Shakespeare PG. Surface ultrastructure of human dermis and wounds. Br J Plast Surg 1993;46:460–65.
26. Michna H, Hartmann G. Adaption of tendon collagen to exercise. Int Orthoped 1989;13(3):161–5.
27. Edsberg LE. Microstructural evaluation of human epidermal tissue subjected to static versus cyclic normal pressures (dissertation). Buffalo, NY: State University of New York at Buffalo; 1994.
28. Edsberg LE, Mates RE, Baier RE, Lauren M. Mechanical characteristics of human epidermal tissue subjected to static versus cyclic pressures. J Rehabil Res Dev 1999;36(2):133–41; http://www.vard.org/jour/99/36/2/edsbe362.htm.
29. Edsberg LE, Natiella J, Baier RE, Earle J. Microstructural characteristics of human epidermal tissue subjected to static versus cyclic normal pressures J Rehabil Res Dev. In press.
30. Campbell JH, Edsberg LE, Natiella JR, Upton G. Biomechanical and histomorphometric properties of healthy and diseased human temporomandibular discs. Jour Oral Maxillofac Surg 1998;56sppl:61.
31. Parry DAD, Barnes GRG, Craig AS. A comparison of size distribution of collagen fibrils in connective tissues as a function of age and a possible relation between fibril size distribution and mechanical properties. Proc R Soc Lond B Biol Sci 1978;203:305–21.
32. Gibson T, Kenedi RM, Craik JE. The mobile micro-architecture of dermal collagen. Br J Surg 1965;52:764–70.
33. Daly CH. Biomechanical properties of dermis. J Investigat Derm 1982;79:17s–20s.
34. Dunn MG, Silver FH. Viscoelastic behavior of human connective tissues: relative contribution of viscous and elastic components. Conn Tiss Res 1983;12(1):59–70.
35. Sangeorzan BJ, Harrington RM, Wyss CR, Czerniecki JM, Matsen FA. Circulatory and mechanical response to skin loading. J Orthopaed Res 1989;7:425–31.
36. Goldstein B, Sanders J. Skin response to repetitve mechanical stress: A new experimental model in pig. Arch Phys Med Rehab 1998;79:265–72.

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