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The Quasi-Linear Viscoelastic Properties of Diabetic and Non-Diabetic Plantar Soft Tissue

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Abstract

The purpose of this study was to characterize the viscoelastic behavior of diabetic and non-diabetic plantar soft tissue at six ulcer-prone/load-bearing locations beneath the foot to determine any changes that may play a role in diabetic ulcer formation and subsequent amputation in this predisposed population. Four older diabetic and four control fresh frozen cadaveric feet were each dissected to isolate plantar tissue specimens from the hallux, first, third, and fifth metatarsals, lateral midfoot, and calcaneus. Stress relaxation experiments were used to quantify the viscoelastic tissue properties by fitting the data to the quasi-linear viscoelastic (QLV) theory using two methods, a *traditional frequency-insensitive* approach and an *indirect frequency-sensitive* approach, and by measuring several additional parameters from the raw data including the rate and amount of overall relaxation. The stress relaxation response of both diabetic and non-diabetic specimens was unexpectedly similar and accordingly few of the QLV parameters for either fit approach and none of raw data parameters differed. Likewise, no differences were found between plantar locations. The accuracy of both fit methods was comparable, however, neither approach predicted the ramp behavior. Further, fit coefficients varied considerably from one method to the other, making it hard to discern meaningful trends. Future testing using alternate loading modes and intact feet may provide more insight into the role that time-dependent properties play in diabetic foot ulceration.

Keywords

Foot; Subcutaneous; Compressive; Stress relaxation; Quasi-linear; Diabetes; Adipose; Ulcer; Viscoelastic; Heel pad

INTRODUCTION

Diabetes has been shown to increase the risk of plantar ulceration, and subsequently a disproportionate amount of amputations occur in this population.⁵ In order to improve treatment options, a better understanding of changes that occur in the presence of this

disease from both a pathological and biomechanical standpoint is needed. Our group and several others have examined diabetes-induced changes in the elastic parameters of the plantar soft tissue.^{7,14,18–21,25,34,37} There have only been a few studies of the viscoelastic behavior of plantar tissue specimens through stress relaxation experiments,^{28,30,32} but these studies have not examined diabetic tissue. In fact, we are only aware of one study that examines the time-dependent visco-elastic properties of diabetic vs. non-diabetic tissue,⁶ yet this study used nerve tissue, not plantar soft tissue. The viscoelastic properties in diabetic plantar tissue represent one aspect of the mechanical properties and are important to quantify as their deterioration may be a potential cause of ulcer formation that could be countered. While we are unaware of any evidence connecting ulcer formation and viscoelastic property changes, it has been argued that viscoelastic insoles may offer protection against plantar ulcer formation,²⁷ possibly by compensating for any loss in tissue performance due to disease. Thus, this study is exploratory in determining what the loss in properties is, if any. Stress relaxation tests provide a means of quantifying and comparing the time-dependent behavior of tissues by fitting the relaxation data to an appropriate viscoelastic model.

Fung's quasi-linear viscoelastic (QLV) theory¹² is a widely used viscoelastic model that provides meaningful phenomenological fit coefficients and has previously been applied to many biological soft tissues, including the plantar soft tissue.^{28,30} The basic premise of this theory is that the strain-dependent and time-dependent properties are separable as defined by an elastic function that yields elastic coefficients and a reduced relaxation function that yields viscous coefficients. The QLV theory has been modified over the years such that there are many implementation approaches to be considered. A widely used approach is the *indirect* method whereby only the relaxation data are used to solve for the elastic and viscous coefficients simultaneously.^{11,15,22,26,28,30,44} This method is beneficial due to its relative simplicity, however, it is sensitive to initial guesses for coefficients which may yield non-unique solutions.^{1,28} Recent alternate methods may offer a less variable approach to determining coefficients, including the *strain-history* approach whereby both the ramp and hold portions of the experiment are utilized,¹ the *direct* fit approach which is similar to the *strain-history* approach except the actual rather than theoretical applied strain is used,⁹ and the *fast convolution* approach which is also similar to the *strain-history* approach except the characteristic convolution integral is evaluated in the frequency rather than time domain.⁶ Limitations of these methods are that they use complex custom algorithms and/or may also be computationally expensive. A *traditional* approach, as coined by Doehring *et al.*⁹ has been to fit the stress–strain ramp data to an elastic function, the stress–time hold data to the reduced relaxation function, and thereby separately obtain the elastic and viscous coefficients.^{41,42,45,46}

Further, within these various QLV theory approaches, different forms of the elastic function and reduced relaxation function may be utilized. For the elastic function in many cases, including the plantar tissue, an exponential function works well.^{3,13,26,28,30,45} In other cases, a power series⁴⁶ or linear function²³ suffices. For the reduced relaxation function, many choose a *frequency-insensitive* function^{11,15,22,26,28,44} although some studies use an exponential function.^{3,13} Others use a *frequency-sensitive* function as defined by a variable amplitude relaxation spectrum.^{23,30} Ideally, the choice of approach for applying the QLV theory to compare diabetic and non-diabetic tissue properties would be simple to implement and sufficiently describe both the ramp and relaxation behavior. While none of the various methods presented are ideal, many offer different aspects that could be combined to adequately quantify diabetic plantar tissue viscoelasticity.

Thus, the purpose of this study was to characterize the viscoelastic behavior of both diabetic and non-diabetic plantar tissue at relevant locations beneath the foot using approaches based on previous implementations of the QLV theory as well as several parameters measured

directly from the raw relaxation data since the fitting process is a potential source of error. These properties are essential to fully understand the role, if any, that viscoelastic property changes play in ulcer formation in diabetic patients and to take necessary measures to prevent amputation in this predisposed populace.

MATERIALS AND METHODS

Experimental Approach

In accordance with a tandem study,³⁴ plantar tissue specimens were obtained from eight fresh frozen cadaveric feet, four diabetic (20.3 ± 8.1 years post-diagnosis) and four non-diabetic, from donors of similar age and weight based on a two-sample *t*-test (Table 1). All feet were harvested within 24 h postmortem and kept frozen until thawing overnight for testing. Six specimens were obtained from each foot at locations subject to loading and ulceration, namely the hallux, first, third, and fifth metatarsal heads, lateral midfoot, and calcaneus (Fig. 1a). The plantar soft tissue was dissected free from the underlying muscle and bone, cut into cylindrical specimens using a 1.905-cm diameter punch, further dissected from the skin (Fig. 1b) to maintain *in vivo* thickness (3 to 11 mm, depending on location), and stored on ice until immediately prior to testing. Each foot was dissected and tested the same day (i.e., one foot per day), and specimen testing order was randomized to minimize any effect due to time between dissection and testing.

Since tissue properties are most meaningful under biomechanically realistic loading that is experimentally repeatable, uniaxial unconfined compression tests were modified to constrain the tissue specimens at both ends to emulate the *in vivo* bone and skin boundary conditions. Each specimen was placed between two platens covered with 220 grit sandpaper and in an environmental chamber near 100% humidity and at 35°C to emulate *in vivo* conditions. This set-up (details shown in our previous study³⁴) was attached to an Electro-Force 3200 materials testing machine (Bose Corporation, Minnetonka, MN). Initial thickness of each specimen was measured using calipers after applying a 0.1-N compressive load. A biomechanically realistic target load based on specimen area, donor weight, normative ground reaction force and contact area,²⁹ and isolation effects from dissecting surrounding tissue away³¹ was used to determine the target displacement. Specifically, the target load was calculated to be 0.075 times body weight by multiplying the specimen area (2.85 cm²) by the average pressure beneath the foot (0.05 times body weight/cm²) and dividing by a factor of 1.9 to account for the estimated effects of specimen isolation since the pressure data were measured in intact feet. All locations were tested to the same target load for each donor. In load control, the specimen underwent ten 1 Hz sine waves from 10 N to the target load; the maximal absolute displacement was noted as the target displacement. Target strain was calculated as target displacement divided by the initial thickness. The sample was allowed to recover in an unloaded state for 10 min followed by a brief tuning period. Specimens were then tested in displacement control by preconditioning with ten 1 Hz sine waves to the target displacement followed by a ramp and hold stress relaxation test to the target displacement. Target ramp and hold times were 0.1 and 300 s, respectively, hence the ramp portion of the test had a target loading rate equivalent to 5 Hz. Strain rate $\dot{\epsilon}$, which varied depending on specimen initial thickness and target strain, and actual ramp time t_0 were recorded. Data were acquired at 1 kHz (i.e., >300,000 data points) and then down-sampled, similar to previous methods,⁹ to 200 points using force separated data to maintain the characteristic curve shape. The resulting relaxation data were normalized by peak force to generate stress–time data and fit to two versions of the QLV theory, a *traditional frequency-insensitive* fit and an *indirect frequency-sensitive* fit (see “Theory” section below), using least squares regression with Igor Pro (Wavemetrics, Lake Oswego, OR). The results from the hold behavior (stress–time relaxation data) were then used to predict the ramp behavior (stress–time ramp data) by substituting the coefficients obtained from the

QLV formulation for the hold ($t = t_0$ to $t = 300$) to the ramp ($t = 0$ to $t = t_0$). Additionally, several characteristic parameters were obtained using the raw force–time data prior to down-sampling as an alternate means of assessing differences between groups since the fitting process is a potential source of error. These included the slopes of the curves to quantify the rate of relaxation at three time intervals (initial slope, $t = t_0$ to $t = t_0 + 0.5$; mid slope, $t = 10$ to $t = 15$; end slope, $t = 290$ to $t = 300$) and the area under the curves after normalization by specimen peak force to compare relative total relaxation.

Theory

The QLV theory assumes the elastic and time-dependent properties are separable and uses a linear combination of these non-linear terms to describe the resultant stress (Eq. (1)), where $G(t)$ is the reduced relaxation function dependent on time t and $\sigma^e(\varepsilon)$ is the elastic function that is dependent on strain ε .¹²

$$\sigma(t, \varepsilon) = \int_0^t G(t - \tau) \frac{\partial \sigma^e(\varepsilon)}{\partial \varepsilon} \frac{\partial \varepsilon}{\partial \tau} d\tau. \quad (1)$$

The reduced relaxation function (Eq. (2)) is defined in terms of the relaxation spectrum $S(\tau)$ (Eq. (3)), where C_1 , τ_1 , and τ_2 are viscous coefficients that describe the amplitude of the viscous effects and the time values corresponding to the frequency limits of the relaxation spectrum, respectively.

$$G(t) = \frac{1 + \int_0^\infty S(\tau) e^{-t/\tau} d\tau}{1 + \int_0^\infty S(\tau) d\tau}, \quad (2)$$

$$S(\tau) = \begin{cases} \frac{C_1}{\tau} & \text{for } \tau_1 \leq \tau \leq \tau_2 \\ 0 & \text{for } \tau < \tau_1, \tau > \tau_2 \end{cases}. \quad (3)$$

A non-linear elastic function⁴⁵ was chosen (Eq. (4)), where A and B are elastic coefficients.

$$\sigma^e(\varepsilon) = A(e^{B\varepsilon} - 1). \quad (4)$$

Two different implementations of the QLV theory were used, namely a *traditional frequency-insensitive* fit and an *indirect frequency-sensitive* fit. The first difference between the fit methods was the approach used to solve for the coefficients. The *traditional frequency-insensitive* approach was based on the *traditional* approach used by Doehring *et al.*⁹ We fit the stress–strain ramp data with the elastic function to determine the elastic coefficients A and B . We then fit the stress–time relaxation data with the QLV theory to determine the viscous coefficients C_1 , τ_1 , and τ_2 while fixing A and B . For the *indirect frequency-sensitive* fit, we used the *indirect* approach²⁶ whereby all the coefficients were solved for simultaneously by fitting the full QLV theory to the ramp data.

The second difference between the *traditional frequency-insensitive* and *indirect frequency-sensitive* fits was the form of relaxation spectrum used (Eqs. (3) and (5)). The *frequency-insensitive* relaxation spectrum has constant viscous effects for all frequencies, while the *frequency-sensitive* relaxation spectrum has variable viscous effects for all frequencies

which are accounted for by an additional viscous coefficient C_2 .²³ The variable amplitude spectrum was introduced since it is capable of capturing the non-linearities seen on a semilog plot of the relaxation data.

$$S(\tau) = \begin{cases} \frac{C_1}{\tau} + \frac{C_2}{\tau^2} & \text{for } \tau_1 \leq \tau \leq \tau_2 \\ 0 & \text{for } \tau < \tau_1, \tau > \tau_2 \end{cases} \quad (5)$$

Statistical Methods

Linear mixed effects regression was used to assess differences in stress relaxation coefficients and raw data parameters by condition (diabetic vs. non-diabetic) or plantar location (calcaneus vs. other). Stress relaxation coefficients (A , B , C_1 , C_2 , τ_1 , τ_2) and raw data parameters (initial, mid, and end slopes as well as normalized area) were the dependent variables, while condition or plantar location was the independent fixed effect, and subject was the random effect. Additional models were carried out with either $\dot{\epsilon}$, t_0 , or peak force F as covariates to account for potential confounding that these variables may have in the association between the stress relaxation coefficients and raw data parameters and condition or plantar location. Significance was set at $p < 0.05$. Analyses were carried out using R 2.9.1 (R Foundation for Statistical Computing, Vienna, Austria).⁴⁰

RESULTS

In general, the stress relaxation response for both diabetic and non-diabetic specimens was similar and exhibited a very rapid relaxation within the first 0.2 s to approximately 70% of the peak stress, with much slower relaxation after this time to approximately 20% of the peak stress after 300 s (Fig. 2). The specimens experienced similar overall strains of $50 \pm 6\%$. Few of the QLV parameters for both the *traditional frequency-insensitive* and *indirect frequency-sensitive* methods (Table 2) or the raw data parameters (Table 3) differed with diabetes status, and these differences for the most part were further reduced when adjusting for disparities in $\dot{\epsilon}$, t_0 , and peak force. For example, B and τ_1 differed for the *traditional frequency-insensitive* fit by diabetes status before adjusting for $\dot{\epsilon}$ and t_0 , but these differences were lost or only borderline significant after adjusting for $\dot{\epsilon}$ and t_0 (Table 2). Similarly, τ_1 differed to a greater extent for the *indirect frequency-sensitive* fit by diabetes status before vs. after adjusting for $\dot{\epsilon}$ and t_0 . Additionally, the coefficients obtained using each fit method varied from one another considerably, e.g., A differed by six orders of magnitude between the *traditional frequency-insensitive* and *indirect frequency-sensitive* fits and the non-significant trends by diabetes status for τ_2 were reversed (the *traditional frequency-insensitive* predicted a longer time till steady state for the diabetic group whereas, the *indirect frequency-sensitive* predicted the opposite).

The stress relaxation response across locations was similar (Fig. 3), and as such, there were almost no significant differences between QLV parameters for both the *traditional frequency-insensitive* and *indirect frequency-sensitive* fits (Table 4) or the raw data parameters (Table 5) between the calcaneus and all other locations tested. The only difference after adjusting for $\dot{\epsilon}$ was seen for C_2 for the *indirect frequency-sensitive* fit but even this difference was lost after adjusting for t_0 . Most areas had similar donor variability, as demonstrated by the standard deviation of the average data (Fig. 4), except for the third metatarsal which had the least donor variability. Again, the coefficients obtained using each fit method (Table 4) varied from one another considerably.

The predictive ability of both the *traditional frequency-insensitive* and *indirect frequency-sensitive* fit methods was similar. The stress relaxation behavior predicted by the average coefficients from both fit methods matched well with the actual average data for both the

diabetic and non-diabetic specimens and was accurate within one standard deviation (Fig. 5). However, neither fit method was accurate in predicting the stress–time ramp behavior, as seen in a sample plot (Fig. 6a). The *traditional frequency-insensitive* fit at least captured the non-linearity of the stress response, whereas the indirect *frequency-sensitive* approximated the ramp to be nearly linear. The non-linear elastic function (Eq. (4)) used to determine A and B for the *traditional frequency-insensitive* fit effectively captured the stress–strain response (Fig. 6b). Overall, both fit methods appeared to adequately fit the relaxation data (Fig. 6c), as determined by minimizing the χ^2 value used to determine the goodness of fit in Igor. The *traditional frequency-insensitive* fit resulted in a poorer fit compared to the indirect frequency-sensitive fit as the χ^2 values for each approach were 0.11 ± 0.10 and 0.03 ± 0.02 , respectively.

DISCUSSION

While changes in the mechanical properties of plantar tissues are thought to play a role in diabetic ulceration, many of these property alterations have yet to be characterized. Specifically, the time-dependent viscoelastic properties of the plantar soft tissue in the presence of diabetes have not been previously quantified. The purpose of this study was to explore the viscoelastic properties of isolated diabetic plantar soft tissue specimens and age-matched controls at six relevant plantar tissue locations. Based on a review of the literature, two approaches to implementing the QLV theory were used.

Interestingly, almost no differences were found between the diabetic and non-diabetic specimens using either fit approach or the raw data parameters. This result was unexpected as subsequent mechanical tests of the stress–strain characteristics conducted immediately after the relaxation tests on the same specimens as used in this study demonstrated differences.³⁴ Further, stress relaxation tests on diabetic nerve tissue have shown altered properties,⁶ hence we expected to see differences in the plantar soft tissue as well. Instead, the time-dependent mechanical properties of the plantar soft tissue in diabetic and non-diabetic feet were similar and thus these properties may be less likely to contribute toward ulceration. Although our analysis is limited for the fitted data since the fitting process is a source of error, the findings are consistent with the raw data parameters which present a more accurate estimation of differences between groups. Further, we can qualitatively see that the relaxation curves from both groups are similar as they overlap (Fig. 2).

In terms of plantar tissue location, few differences were found between groups. This result is consistent with our previous findings of the stress–strain characteristics³⁴ and possibly indicates that any differences between locations that increase the risk of ulceration occur at a structural level (i.e., in intact feet rather than isolated specimens) or under different loading regimes (e.g., shear loading). Additionally, the variation between donors was small (per the standard deviations for each individual location, Fig. 4) even though specimens were pooled irrespective of disease status, further indicating similarities between the properties of diabetic and non-diabetic tissues.

We summarized the fit approaches considered along with their respective rationale and limitations (Table 6). It should be noted that there are of course many other custom non-linear viscoelastic models of soft tissues that could potentially be applied to the plantar tissue^{4,10,17,33,36,38,39} but were not considered for this study for simplicity and since our initial hope was to compare our work with previous characterizations. Hence, the QLV theory was chosen based on its previous use to successfully describe young, healthy plantar soft tissue whereby an *indirect frequency-insensitive* fit method was employed.²⁸ This approach was limited for the present study due to its sensitivity to initial guesses for coefficients, resulting in non-unique solutions and making comparisons between groups

unreliable. To improve convergence, the *traditional frequency-insensitive* method was used; however, this approach was limited as the data were found to be non-linear on a semi-log plot. As such, a variable amplitude relaxation spectrum capable of capturing this non-linearity was introduced based on previous methods used to describe frequency-sensitive behavior.^{23,30} This approach constituted a *traditional frequency-sensitive* method, however, fixing A and B with the introduction of the additional coefficient C_2 resulted in a poor, non-convergent fit (i.e., the fit curve was not close to the experimental data after many attempts using different initial guesses for coefficients). Hence, we reverted back to the indirect approach while maintaining a variable amplitude spectrum using an *indirect frequency-sensitive* method. Of note, we did not try to incorporate the *strain-history/direct* fit approaches^{1,9} with *frequency sensitivity*.²³ Further, although it is likely that the traditional frequency-insensitive fit better predicted the non-linearity of the stress–time ramp behavior because the elastic coefficients were directly solved for from the ramp data, we did not explore alternate elastic functions that might improve the accuracy of this prediction.

The differences between coefficients from each of the fit approaches are to be expected given that both methods effectively utilized different constitutive equations, even if they were based on the same QLV theory. As a result, the coefficient values obtained are not absolute making comparisons between methods irrelevant. Although the phenomenological meaning of the coefficients likely varies by fit method as well, in general C_1 , C_2 , τ_1 , and τ_2 are viscous coefficients that describe the amplitude of the viscous effects and the time values corresponding to the frequency limits of the relaxation spectrum, respectively, and A and B are elastic coefficients that describe the non-linear elastic properties. Although there were few differences between groups for the *traditional frequency-insensitive* fit, B was significantly higher for the diabetic tissue before adjusting for $\dot{\epsilon}$ and t_0 , indicating stiffer tissue consistent with our findings from the tandem study.³⁴ Further, τ_1 was greater in the diabetic tissue indicating a longer initial relaxation, possibly due to an inability of the tissue to respond as quickly as the healthy tissue. This finding was similar for the *indirect frequency-sensitive* fit as τ_1 was greater in the diabetic group both before and after adjusting for $\dot{\epsilon}$ and t_0 .

Comparison of the obtained coefficients to previous approximations for plantar tissue is difficult due to differences in the aforementioned theoretical as well as experimental methods. Ledoux *et al.* examined the properties of plantar tissue from young healthy rather than older diabetic donors, assumed frictionless boundary conditions, and used an *indirect frequency-insensitive* fit.²⁸ Miller-Young also assumed frictionless boundary conditions, used different loading rates, and used a custom modification of a hyperelastic constitutive model³² hence it is not possible to compare coefficients.

It seems unlikely that the viscoelastic tissue properties of the plantar tissue alone play a role in diabetic ulcer formation given the limited differences between the diabetic and non-diabetic results. We had previously calculated energy loss using stress–strain hysteresis curves as one measure of viscoelasticity³⁴ and were surprised to find no differences by disease status given that other tests of diabetic tissue at a structural level indicate increased energy loss.^{18,20,21} We chose to quantify the time-dependent viscoelastic properties of the plantar soft tissue using stress relaxation tests as another measure for comparison between the diabetic and non-diabetic groups yet we again did not find differences between groups. Based on our present findings at a material level and previous findings at a structural level, it seems plausible that viscoelastic property changes may only occur at a structural level since they do not manifest in the plantar tissue alone.

There were some potential limitations in this study. Diabetic and non-diabetic specimens were tested at different strain rates and ramp times. However, we attempted to account for

these differences in the statistical analysis. A closer examination of two specimens with the most different ramp times demonstrated that this effect was a result of difficulties in tuning the testing machine (Fig. 7). Although all testing was done by the same person and significant time was spent tuning, diabetic specimens were inherently more difficult to tune as evidenced by the increased ramp time. Tuning duration had to be limited in such cases to avoid specimen damage. Despite an increased ramp time, we were at least able to minimize target strain errors through tuning to 0.3% which has been shown to result in a 3% error on the measured forces.³⁵ The raw data parameters were limited as they represent only a few distinct parts of the relaxation curve as it was not feasible to compare each of the 300,000 data points for the 48 specimen relaxation curves directly while accounting for differences due to foot, plantar location, peak force, ramp time, and strain rate. Further, we only performed a limited analysis of the predictive capabilities of the QLV coefficients and did not test the tissue to different strain levels. Moreover, although we only allowed the tissue to relax for 300 s to minimize specimen fatigue, our QLV approach does not assume that steady state has been achieved and solves for the long-term time constant τ_2 rather than fixing it to the test duration. Note that the goodness of fit, as measured by the χ^2 value, is just one way to compare fitting models and does not account for complexity due to a differing number of material parameters, as offered by the Akaike Information Criterion (see, e.g., Schmid *et al.*⁴³). Additionally, as we previously noted,³⁴ we did not test tissue from the digits despite their susceptibility to ulceration^{8,24} due to difficulties in dissecting such small tissue sections. It is also possible that some of the diabetic feet may not have undergone tissue changes even after ~15 years of hyperglycemia, although this risk is low given that diabetes diagnosis may occur 9–12 years after onset,¹⁶ hence we are underestimating disease duration. Further, the area used to calculate stress was based on the punch diameter as we assumed the tissue specimen diameter did not change based on the minimal visible retraction of the tissue. Finally, although we utilized fresh frozen cadaveric rather than living tissue, freshly amputated heel pads have been shown to have similar properties to pads that have previously been frozen.²

This work demonstrates that few changes with diabetes in the viscoelastic properties of the plantar soft tissue are observed. Further studies, such as shear or structural testing, may provide more insight into the role that time-dependent properties play in diabetic foot ulceration. Additionally, other viscoelastic models as well as QLV theory approaches that incorporate the *strain-history/direct* fit methods with a variable amplitude spectrum should be considered to improve the convergence and predictive ability of the model.

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FIGURE 1.

Foot dissection showing (a) specimen locations where ha = hallux, m1, m3, and m5 = first, third, and fifth metatarsals, la = lateral midfoot, and ca = calcaneus, as well as (b) a typical plantar tissue specimen during skin removal.

FIGURE 2. Normalized stress vs. log time plots comparing average relaxation data for diabetic (D) and non-diabetic (N) specimens.

FIGURE 3.

Normalized stress vs. log time plots comparing average relaxation data for all plantar locations where ha = hallux, m1, m3, and m5 = first, third, and fifth metatarsals, la = lateral midfoot, and ca = calcaneus (note that standard deviations are shown in Fig. 4).

FIGURE 4.

Normalized stress vs. log time plots showing average relaxation data and standard deviations for individual plantar locations where ha = hallux, m1, m3, and m5 = first, third, and fifth metatarsals, la = lateral midfoot, and ca = calcaneus.

FIGURE 5. Normalized stress vs. log time plots for (a) diabetic (D) and (b) non-diabetic (N) specimens showing average relaxation data and predictions using average coefficients from both fit methods (TFI = *traditional frequency-insensitive* and IFS = *indirect frequency-sensitive*).

FIGURE 6.

Sample normalized stress plots showing (a) predictions of the stress–time ramp data using coefficients from both fit methods as well as (b) the corresponding fit of the non-linear elastic function to the stress–strain ramp data and (c) the actual fit of the relaxation stress–time hold data (TFI = *traditional frequency-insensitive* and IFS = *indirect frequency-sensitive*).

FIGURE 7.

Normalized stress and strain vs. time plot showing two specimens with the most different ramp times (m3N4 and m3D2 represent the best and worst tuned specimens, respectively). Deviations between the actual (t_0) and the target (0.1 s) ramp times may confound differences in the stress response between groups and have thus been accounted for (Tables 2, 3).

TABLE 1

Mean [SD] donor information.

	Diabetic	Non-diabetic	<i>p</i> [*]
Age (years)	70 [8]	68 [5]	0.6
Weight (kg)	94 [25]	70 [12]	0.15
Gender (M:F)	2:2	2:2	—

*
 $p < 0.05$ for two-sample *t*-test.

TABLE 2

Mean [SD] QLV stress relaxation curve fit coefficients by diabetes status.

	Diabetic (<i>n</i> = 4 feet, 24 specimens)	Non-diabetic (<i>n</i> = 4 feet, 24 specimens)	<i>p</i> * <i>p</i> ** <i>p</i> ***
$\epsilon'(1/s)$	3.33 [0.59]	4.10 [0.62]	0.0029
t_0 (s)	0.151 [0.029]	0.123 [0.011]	0.0083
Traditional frequency-insensitive fit			
<i>A</i> (Pa)	1.05 [1.17]	1.72 [1.96]	0.2/0.3/0.6
<i>B</i>	25.7 [4.0]	22.8 [3.5]	0.012/1.0/0.12
<i>C</i> ₁	2.01 [2.53]	0.96 [1.31]	0.3/0.5/0.4
τ_1 (s)	0.043 [0.029]	0.012 [0.012]	0.0057/0.046/0.064
τ_2 (s)	1479 [3522]	426 [678]	0.4/0.3/0.2
Indirect frequency-sensitive fit			
<i>A</i> (Pa)	100e+6 [104e+6]	49e+6 [109e+6]	0.094/0.5/0.3
<i>B</i>	0.05 [0.17]	0.45 [0.68]	0.13/0.3/0.2
<i>C</i> ₁	0.81 [0.20]	0.66 [0.20]	0.072/0.8/0.9
<i>C</i> ₂	0.109 [0.073]	0.099 [0.045]	0.6/0.2/0.3
τ_1 (s)	0.046 [0.021]	0.021 [0.009]	0.0003/0.0008/0.0009
τ_2 (s)	469 [658]	1016 [960]	0.14/0.4/0.5

* $p < 0.05$ for linear mixed effects regression with random effect for foot** adjusted for ϵ' *** adjusted for t_0 .

TABLE 3

Mean [SD] raw data parameters obtained from force–time relaxation curves by diabetes status.

	Diabetic (<i>n</i> = 4 feet, 24 specimens)	Non-diabetic (<i>n</i> = 4 feet, 24 specimens)	p^* p^{**} p^{***}
Peak force (N)	32.2 [7.7]	20.2 [5.0]	0.0032
Peak strain (%)	49.5 [5.9]	50.1 [5.8]	0.6
Initial slope (N/s)	−40.6 [15.4]	−53.0 [14.3]	0.016/0.8/0.3
Mid slope (N/s)	−0.24 [0.07]	−0.13 [0.05]	0.0042/0.0086/0.2
End slope (N/s)	−0.0049 [0.0032]	−0.0023 [0.0033]	0.0082/0.013/0.11
Normalized area (N s/N)	59 [20]	66 [16]	0.4/0.6

* $p < 0.05$ for linear mixed effects regression with random effect for foot

** adjusted for ϵ

*** adjusted for peak force.

TABLE 4

Mean [SD] QLV stress relaxation curve fit coefficients by location (all others vs. calcaneus).

	Other (<i>n</i> = 8 feet, 40 specimens)	Calcaneus (<i>n</i> = 8 feet, 8 specimens)	<i>p</i> * / <i>p</i> ** / <i>p</i> ***
ϵ' (1 / s)	3.63 [0.72]	4.15 [0.53]	0.014
t_0 (s)	0.139 [0.027]	0.125 [0.014]	0.058
Traditional frequency-insensitive fit			
<i>A</i> (Pa)	1.41 [1.75]	1.22 [0.91]	0.7/0.6/0.5
<i>B</i>	24.6 [4.0]	22.5 [3.8]	0.2/1.0/0.4
<i>C</i> ₁	1.48 [2.07]	1.51 [2.17]	1.0/0.6/0.8
τ_1 (s)	0.030 [0.028]	0.017 [0.015]	0.091/1.0/0.9
τ_2 (s)	992 [2791]	755 [843]	0.8/0.6/0.3
Indirect frequency-sensitive fit			
<i>A</i> (Pa)	82e+6 [116e+6]	33e+6 [47e+6]	0.2/0.5/0.4
<i>B</i>	0.23 [0.51]	0.35 [0.67]	0.4/1.0/0.6
<i>C</i> ₁	0.74 [0.22]	0.73 [0.21]	0.9/0.10/0.3
<i>C</i> ₂	0.109 [0.063]	0.079 [0.043]	0.2/0.040/0.1
τ_1 (s)	0.036 [0.021]	0.023 [0.010]	0.034/0.13/0.2
τ_2 (s)	665 [773]	1128 [1195]	0.085/0.3/0.2

* $p < 0.05$ for linear mixed effects regression with random effect for foot** adjusted for ϵ' *** adjusted for t_0 .

TABLE 5

Mean [SD] raw data parameters obtained from force–time relaxation curves by plantar location.

	Other (<i>n</i> = 8 feet, 40 specimens)	Calcaneus (<i>n</i> = 8 feet, 8 specimens)	p^* $/p^{**}$ $/p^{***}$
Peak force (N))	26.4 [8.8]	25.2 [9.5]	0.6
Peak strain (%)	49.2 [5.7]	52.0 [6.4]	0.2
Initial slope (N/s)	−46.2 [16.8]	−49.8 [11.1]	0.5/0.2/0.6
Mid slope (N/s)	−0.19 [0.08]	−0.18 [0.08]	0.7/0.6/0.8
End slope (N/s)	−0.0034 [0.0036]	−0.0044 [0.0030]	0.4/0.5/0.4
Normalized area (N.s/N)	61 [18]	70 [20]	0.097/0.2

* $p < 0.05$ for linear mixed effects regression with random effect for foot

** adjusted for ϵ

*** adjusted for peak force.

TABLE 6

Summary of rationale for the QLV fit approaches used for the plantar soft tissue.

	Indirect		Traditional
Frequency-insensitive	<p>1. <i>Method:</i> All coefficients (B, C_1, τ_1, τ_2) are solved simultaneously from σ-t hold data and the QLV function except A which is determined last by substituting other coefficients into the equation for peak stress.</p> <p><i>Rationale:</i> Previously used for plantar tissue analysis.²⁸</p> <p><i>Limitation:</i> Sensitive to initial guesses leading to non-unique solutions.</p>	→	<p>2. <i>Method:</i> Elastic coefficients (A, B) are solved using σ-ε ramp data and a non-linear elastic function, then substituted into the QLV function to solve for remaining coefficients (C_1, τ_1, τ_2) from σ-t hold data.</p> <p><i>Rationale:</i> Less sensitive to initial guesses, depicts non-linearity of σ-t ramp.</p> <p><i>Limitation:</i> Poorly estimates peak stress and frequency-sensitivity of σ-t hold.</p>
		↓	
Frequency-sensitive	<p>4. <i>Method:</i> Same variable amplitude relaxation spectrum as (3) and approach as (1) whereby all coefficients (B, C_1, C_2, τ_1, τ_2) except A are solved for together from σ-t hold data.</p> <p><i>Rationale:</i> Better depicts shape of σ-t hold, accurately estimates peak stress.</p> <p><i>Limitation:</i> Some sensitivity to initial guesses, poorly estimates shape of σ-t ramp data.</p>	←	<p>3. <i>Method:</i> Same approach as (2), but with a variable amplitude relaxation spectrum whereby elastic coefficients (A, B) from σ-ε ramp data are fixed while solving for viscous coefficients (C_1, C_2, τ_1, τ_2) from σ-t hold data.</p> <p><i>Rationale:</i> Data appeared to be frequency sensitive.</p> <p><i>Limitation:</i> Constraining elastic coefficients resulted in a very poor or non-convergent fit.</p>

Methods 2 and 4 were implemented in this study.