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PROGRESSIVE MECHANICAL BEHAVIOR OF HUMAN CORTICAL BONE IN TENSION FOR TWO AGE GROUPS

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Abstract

The capacity of bone for post-yield energy dissipation decreases with age. To gain information on the cause of such changes, we examined the mechanical behavior of human cadaveric bone as a function of progressive deformation. In this study, tensile specimens from tibiae of 9 middle aged and 8 elderly donors were loaded till failure in an incremental and cyclic (load-dwell-unload-dwell-reload) scheme. The elastic modulus, maximum stress, permanent strain, stress relaxation, viscoelastic time constant, plastic strain energy, elastic release strain energy, and hysteresis energy were determined at incremental strains of each loading cycle. Experimental results showed that elderly bone failed at much lower strains compared to middle aged bone, but little age-related differences were observed in the mechanical behavior of bone until the premature failure of elderly bone. Energy dissipation and permanent strain appeared to linearly increase with increasing strain, while non-linear changes occurred in the modulus loss and stress relaxation/time constant with increasing strain. Such changes suggest that two distinct stages may exist in the progressive deformation of bone. In Stage I, rapid damage accumulation and increased involvement of collagen in load bearing appeared to dominate the mechanical behavior of bone with limited energy dissipation (<20% of total energy dissipated), whereas Stage II is dominated by continuous plastic deformation, accompanied by major energy dissipation through all three pathways till failure. This study suggests that damaging mechanisms in bone vary with deformation and age affects the post-yield mechanisms causing a significant decline in the capacity of aged bone to dissipate energy.

Keywords

Bone; Post-yield; Aging; Energy dissipation; Damage accumulation

INTRODUCTION

There are a number of studies demonstrating that age-related differences in the mechanical properties of bone are associated with changes in bone composition and microstructure.¹⁻³ For

example, an increase in microscopic porosity could lead to the decrease in bone strength with increasing age.¹ In addition, a decline in collagen thermal stability or collagen network integrity has been reported to be a possible factor for the age-related decrease in bone toughness.^{3,4} Given the hierarchical arrangement of bone constituents, a number of factors across multiple length scales (Table 1) may contribute to the mechanical competence of bone (*i.e.*, the resistance to fracture). This structural complexity thus hinders a complete mechanistic explanation (model) for the rise in bone fracture in the elderly. Traditionally, an age-related loss of bone mass has been viewed as the reason for the rising incidence of bone fractures in the elderly, and the success of therapeutic treatments is evaluated, in part, by their ability to increase bone mass.⁵ However, the concept of bone quality has emerged to provide further insight into why individuals with 'normal' bone mineral density (BMD) suffer fractures. This concept recognizes that fatigue microdamage and collagen network integrity, among other inherent characteristics of bone tissue (*e.g.*, BMD), are also important as to whether or not bone is at risk of breaking.^{6,7}

Bone is a hierarchical and hydrated composite of mineral and collagen phases,⁸⁻¹⁰ showing a rather complex response to the mechanical loading.¹¹⁻¹³ While previous research has investigated the resistance of bone to crack propagation,¹⁴⁻¹⁶ fatigue behavior,¹⁷⁻²³ and mechanical changes to load-induced damage,²⁴⁻²⁶ little is known about the age-dependent differences in the mechanical behavior of bone as a function of progressive deformation (strain). Moreover, to the best of our knowledge, there is a paucity of data on the age-related differences in energy dissipation and viscous behavior at any given level of progressive deformation. Such information may be insightful to the identification of certain age-related changes in the tissue that influence bone quality and ultimately its resistance to fracture.

In this study, by employing a previously developed progressive loading scheme,²⁷ we examined the age-related differences in the mechanical behavior of bone between two age groups (middle aged and elderly) against progressive deformation, so as to gain more information on the underlying mechanisms for such differences. We hypothesized that age has an effect on the capacity of bone to deform giving rise to age-related differences in post-yield energy dissipation (*i.e.*, toughness or bone quality).

MATERIALS AND METHODS

Specimen preparation

Seventeen cadaveric tibiae were obtained from the Willed Body Program (The University of Texas Southwestern Medical Center at Dallas, TX) with the stipulation that the donors had no known bone disease. The specimens were divided into two age groups: The middle aged group had bone from 4 female donors of 53, 54, 54, and 56 years and from 5 male donors of 49, 51, 51, 52, and 55 years, while the elderly group had bone from 4 female donors of 84, 88, 88, and 90 years and from 4 male donors of 72, 76, 79, and 87 years. Cut from the anterior quadrant of each mid-diaphysis, a longitudinal strip of bone was machined under hydrated conditions into a tensile specimen such that the osteons ran in the axial direction of loading. The gage region (10 mm in length and 2.1 mm in width) tapered over 5 mm (radius of 20 mm) into the grip regions (10 mm in length and 5 mm in width). The final thickness of the specimen was hand ground to 2.1 mm. All specimens were wrapped in gauze, soaked in phosphate buffered saline, and stored at -20 °C until time of testing.

Mechanical Testing

We recently developed a new method for assessing bone quality through quantification of post-yield energy dissipation of bone in tension²⁷ and found that energy dissipation was associated with collagen content and non-enzymatic cross-links and that it decreased with age.²⁸ Like

previous studies on the effect of load-induced damage on mechanical properties,^{11,24-26} this method involves loading, unloading, and reloading the bone. Unlike the earlier work, it subjects bone specimens to multiple bouts of the loading cycle, in which deformation increases incrementally with each cycle and equal periods of dwell are inserted between each change in loading direction (Fig. 1). Such a scheme provides a means to track changes in the mechanical properties of bone as a function of incremental strain (*i.e.*, progressive deformation). This approach can provide the following advantages: 1) post-yield energy dissipation can be partitioned into different pathways, 2) elastic, plastic, and viscous behaviors can be assessed as a function of progressive deformation, and 3) such information could potentially help formulate the constitutive model of the tissue.

As previously described,^{27,28} the cortical specimens were tested in tension following a progressive load-dwell-unload-dwell-reload scheme. Using an EnduraTEC ELF 3300 (Bose Corporation, Minnetonka, MN), each specimen was loaded at 0.5 mm/min to an initial cross-head displacement of 0.05 mm, held at the level of 0.05 mm for 30 seconds (stress relaxation), unloaded at 300 N/min to zero force, held for 30 seconds at zero force (anelastic relaxation), and reloaded at 0.5 mm/min to the next displacement level with an increment of 0.05 mm. This procedure was repeated until failure (Fig. 1A). The dwelling time (*i.e.*, 30s) was determined by pilot tests and was found to be long enough for the viscoelastic response to reach equilibrium state. During the displacement control dwell, the viscoelastic response of bone specimens was evaluated. Elongation (δ) was recorded by an extensometer (MTS 632.26F-20, 8 mm gage, Eden Prairie, MN) at a gage length (L) of 8 mm, and the strain value in the gage region was calculated accordingly (*i.e.*, δ/L). Hydration was maintained by dripping distilled water on the loaded specimen throughout the test.

Quantification of mechanical properties

The following properties were quantified at each progressive strain level (or loading cycle) as shown in Fig 1: 1) the modulus (E_i) was estimated as the slope between the points at the end of stress relaxation dwelling and at the end of anelastic deformation dwelling; 2) the maximum stress ($\sigma_{\max,i}$) was determined at the maximum strain in the cycle; 3) the permanent strain ($\epsilon_{p,i}$) was the residual strain value after anelastic deformation and before reloading; 4) the stress relaxation ($\Delta\sigma_i$) was quantified as the percent change in stress from the beginning to the end of the stress relaxation dwelling period (*i.e.*, approaching equilibrium) and the viscoelastic time constant (τ) was estimated by fitting the stress-time curve during the dwelling with an exponential equation ($\sigma_i + \Delta\sigma \cdot e^{-t/\tau}$); and 5) the post-yield energy dissipation terms ($U_{p,i}$, $U_{er,i}$, $U_{h,i}$) were the areas between or under the loading/unloading curves and under the slope for determining the nominal elastic deformations (Fig. 1A).

These properties were calculated for each incremental cycle by a custom Matlab script (v7.0.1, The Mathworks, Inc., Natick, MA), in which the areas under curves were determined by Simpson's 1/3rd rule.²⁹ In fact, there is an overlap between adjacent cycles: That is, the reload of the current cycle is also the first step of the next cycle, and the end of the current cycle occurs where the reload curve crosses over the first dwell curve (stress relaxation $\Delta\sigma_i$ in Fig. 1). By plotting the measured properties against the progressive strain (ϵ_i), variation of material properties of bone with the progressive deformation were obtained for both age groups. Fig. 1B represents an example of the relationship between $\Delta\sigma_i$ and the progressive strain determined using the aforementioned approach. The stress-strain behavior under monotonic loading could be estimated as the envelope of the cyclic stress-strain curve for each specimen (Fig. 1A). Lastly, the yield strain (ϵ_y) and transition strain (ϵ_T) were determined for each specimen. The former was defined as the ϵ_i at which permanent deformation ($\epsilon_{p,i}$) starts to occur (Fig. 3), while the latter was estimated to be the ϵ_i at the peak stress relaxation ($\Delta\sigma_T$).

Statistical analysis

The statistical analyses of experimental data were performed at pre-defined strain ranges based on the different deformation stages, which are described later (Table 2). The mean and variance of the applied strains for the middle aged and elderly bones were found to be statistically consistent in each deformation stage (Table 3). At these different deformation stages, the age-related effect on the bone properties (ϵ_i , $\epsilon_{p,i}$, $\Delta\sigma_i$, τ_i , E_i , $\sigma_{\max,i}$, $U_{p,i}$, $U_{cr,i}$, and $U_{h,i}$) were examined applying Bootstrap two-sample, one-sided or two sided *t*-test (MULTTEST Procedure, SAS/STAT User's Guide version 9, 2004, SAS Institute Inc., Cary, NC). The Bootstrap method is a robust computer-intensive re-sampling technique providing an alternative statistical inference that is not as sensitive to errors in the assumed model. Bootstrap methods are generally used for small data sets or where sample distributions are non-normal. The same statistical method was used to test whether there were age-related differences in bone properties when quantified in the last cycle before failure (Table 4). The effect of age on ϵ_y , ϵ_T , and $\Delta\sigma_T$ was also examined. The statistical difference was considered only if $p < 0.05$.

RESULTS

Overall, we observed consistent (if not identical) trends in the changes of all material properties of bone with increasing strain for both age groups (Figs. 1B & 2-6). Statistical analyses also showed that age had little effects on the mechanical behavior of bone over the similar deformation ranges (Table 3). The major difference was that the elderly bone specimens failed prematurely at much less strain compared with the middle-aged ones, which resulted in significant age-related differences in bone properties quantified at the last cycle before failure (Table 4). Moreover, yield strain (ϵ_y) appeared to slightly decrease with age, but the transition strain (ϵ_T) and peak stress relaxation ($\Delta\sigma_T$) was not affected by aging (Table 4).

The estimated monotonic stress-strain behavior of bone (via progressive cycle loading) was manifested with an initial linear elastic behavior followed by an almost linear plastic deformation after yielding, in which stress increased at much smaller rate with increasing strain (Fig. 2). The permanent deformation ($\epsilon_{p,i}$) appeared to occur at approximately 0.39%-0.43% strain. Thereafter, a positive linear relationship existed between the plastic strain and the total strain applied to the bone specimens (Fig. 3).

The elastic modulus (E_i) exhibited a continual decrease with increasing strain, showing a sharp drop between the yield and transition strains, followed by markedly reduced rate of decline through post-yield strains (Fig. 4). Comparing the two age groups, elderly bone experienced the initial sharp loss and some of the transient changes of the elastic modulus with increasing strain till failure, whereas middle-aged bone appeared to be able to sustain more modulus loss with much greater post-yield deformation. The maximum modulus loss was about 71% for elderly bone and 85% for middle-aged bone, respectively.

Relatively complex changes were observed in the stress relaxation ($\Delta\sigma_i$) and the viscoelastic time constant (τ_i) against the applied strain (Fig. 1B and Fig. 5). From the perspective of viscoelasticity, the amount of $\Delta\sigma_i$ most likely reflects the relative stiffness of the collagen phase, whereas the value of τ_i could be deemed as an indicator of the viscous response of the collagen phase in bone to loading. Stress relaxation increased linearly to a peak value of $\sim 1.0\%$ strain with a similar rate and magnitude for both age groups (Table 4). Thereafter, a sudden pause in this increase occurred, and a continuous decline followed as deformation exceeded 1.0% strain. Similarly, the time constant (viscous response) dropped sharply till about 1.0% strain, from which it leveled off and became a plateau (a saturated state). Such changes in both $\Delta\sigma_i$ and τ_i suggest that a mechanistic change (transition) in the mechanical behavior of bone occurred, which is most likely related to the viscoelastic behavior of the collagen phase.

The energy dissipation in the all three pathways (*i.e.*, plastic strain, elastic release strain, and hysteresis) measured in this study exhibited approximately linear relationships with the strain applied (Fig. 6). However, the start of U_p and U_{er} dissipation appeared to coincide with the yield strain, whereas U_h developed at a slightly lower strain level ($\sim 0.25\%$). In addition, it was observed that the changing rate of energy dissipation ($\Delta U/\Delta \epsilon$) for U_p was almost twice as great as those of the other two energy terms (U_{er} and U_h). Their contribution to the total energy dissipation ($U_p + U_{er} + U_h$) was estimated to be about 53% for U_p , 26% for U_h , and 21% for U_{er} , respectively.

DISCUSSION

To better understand age-related differences in the post-yield behavior of human cortical bone, we employed a progressive loading scheme that could estimate the mechanical behavior of bone as a function of progressive deformation (strain). The results of this study indicated that the mechanical behavior of cortical bone changed almost identically with increasing strain for both middle-aged and elderly groups except that the former could sustain much greater plastic deformation than the latter (Figs. 2-6), thereby causing age-related differences in a number of mechanical properties (Table 4). In addition, there appeared to be a change in the damaging mechanisms at 1% strain, and age perhaps had effects on the successive mechanisms since bone from elderly did not survive excessive strains after 1%. This change in mechanism is noticeable in both modulus and stress relaxation behaviors in that at the transition the rapid loss in modulus of bone slowed and the increase in stress relaxation of bone peaked (Figs. 1B & 4). Finally, the post-yield energy dissipation and the permanent strain of bone increased almost linearly with increasing post-yield strain (Figs. 3 and 6).

One important finding of the present study is that no significant age-related differences in the mechanical behavior of bone as a function of progressive deformation appeared to exist except that the elderly bone specimens failing at much lower strain levels, thus leading to a decreased toughness (Fig. 6). In the past, the age-related decrease in the toughness of bulk bone specimens under monotonic loading modes has been well reported in the literature.^{1-3,30-32} On the other hand, it has been reported that mechanical properties of bone vary as post-yield deformation proceeds.^{11,28,33} Thus, it is interesting to examine whether or not such changes are also age-dependent. The results of this study clearly demonstrate that no age-related difference in bone mechanical behavior is observable till the early stage of post-yielding, at which the elderly bone fails prematurely. This suggests that the toughening mechanism in bone is similar through elastic and early post-yield deformation for both age groups. However, unlike the younger tissue, the toughening mechanism for elderly bone diminishes abruptly for further post-yield deformation. Previous work has indicated that the increase in the resistance to crack growth as a crack advances (*i.e.*, the rising R-curve) is greater for young bone than elderly bone, implying that age-dependent changes in bone allow for existing cracks to propagate more readily.^{34, 35} In fact, the present study has, for the first time, provided evidence that the age-related difference in the mechanical behavior of bone is mainly reflected in the failure strain of the tissue instead of other mechanical properties.

Another important observation of this study is that the mechanical behavior of bone under progressive deformation is manifested in two successive stages: At the first stage (Stage I as defined in Fig. 1B) that is about 0.4% to 1.0% strain, there is a sharp drop of elastic modulus (Fig. 4), acute changes in viscous responses (*i.e.*, stress relaxation and time constant in Fig. 5), and finally a limited energy dissipation (less than 20% of the maximum total energy dissipation in Fig. 6). In contrast, the second stage (Stage II as defined in Fig. 1B), which is beyond 1.0% strain, is characterized by a significantly reduced decline in the elastic modulus and a saturated or slightly reduced viscous response (τ and $\Delta\sigma$) of the tissue with increasing plastic deformation (Figs. 4 and 5). In fact, the majority of the energy dissipation is realized at Stage II (Fig. 6).

These observations naturally lead to the speculation that two distinct mechanisms may exist in bone, which respectively dominate the early (Stage I) and later (Stage II) deformations. As to aging effects, it is noteworthy that elderly bone would only survive Stage I and early part of Stage II, whereas the middle aged bone could survive with much greater strain in Stage II.

The sharp drop of elastic modulus at Stage I deformation most likely implies an extensive formation of damage in bone because it has been commonly deemed that modulus degradation is an indicator of microdamage accumulation in the tissue.³⁶⁻³⁹ Such an argument has also been used in a number of studies to track damage accumulation in the fatigue of the tissue.^{17,19,21,23,38,40} However, most of these studies did not directly measure the type, size, and number of the damages. In a study by Courtney et al.²⁶, bone specimens from two different age groups were loaded in tension to the same level of post-yield deformation (1% strain). Similar with the result of the present study, no age-related difference was found on modulus loss between the young adults and elderly groups. However, they found that more new microcracks were created in the elderly bone, whereas no such changes but increased crack sizes were observed in the young adult bone. In the present study, both middle-aged and elderly bone specimens exhibited similar progression of modulus loss prior to the premature failure of the elderly ones (Figs. 2-6). However, this may not necessarily reflect the differences in the type, size, and number of the damages between the two age groups.

The acute increase in the $\Delta\sigma$ and sharp decrease in the τ at Stage I suggest that the involvement of the collagen phase in load bearing is markedly elevated because the collagen phase is considered to be the major contributor to the viscoelastic behavior of the tissue.⁴¹⁻⁴³ It is conceivable that fast damage accumulation would have more collagen exposed to load bearing and consequently augment the viscous response in the overall mechanical behavior of bone. Moreover, an increase in the initial non-linearity of the stress-strain behavior (*i.e.*, toe region) has been observed in the collagen matrix of damaged bone (via overloading), suggesting that damage does affect the collagen phase.⁴⁴ Thus, it could be speculated that significant microdamage accumulation in Stage I is a cause of an acute increase of collagen involvement in load bearing. Also interesting is that the stress relaxation and time constant do vary with increasing strain before the plastic deformation takes place, therefore suggesting that the collagen phase is involved in load bearing even during the elastic deformation of bone. Presumably, it is the preexisting damages in bone that contribute to such viscoelastic responses of the tissue at the pre-yielding stage. In addition, previous studies have shown that the viscous properties of bone are more sensitive to damage accumulation in bone than modulus degradation, indicating that the variation in stress relaxation is about 10 times greater than the modulus reduction at a certain degree of post-yield deformation in torsion.³³ However, stress relaxation did not show such great sensitivity in tension as reported in this study, suggesting that the viscous response of bone may be significantly affected by loading modes (*e.g.*, tension vs. torsion).

Limited energy dissipation (less than 20% of the maximum total energy consumption till failure) was observed in Stage I although bone had experienced significant modulus loss and increased viscous responses. Previous studies have suggested that microcracking during damage accumulation may be a toughening mechanism or energy dissipation pathway for bone.⁴⁵⁻⁴⁹ However, the results of this study imply that microcracking itself is not the only major mechanism for energy dissipation. Damage accumulation (Stage I) perhaps serves as a prerequisite for the further energy dissipation in bone (Stage II). Some recent studies proposed that sacrificial bonds and hidden length of interfacial molecules between the mineralized collagen fibrils could also be toughening mechanisms in bone.^{50,51}

Previous studies have reported that yielding of bone is related to damage accumulation.^{31, 40,48} Using piezoelectric transducers, acoustic emission events were detected at the yielding

point during tensile tests of bovine bone.⁴⁷ Similarly, it was found that microcracks were induced at yielding by loading bone specimens in a fluorescein bath under a laser scanning confocal microscope.⁵² Unlike the estimate by those previous studies, the present study demonstrated that modulus loss (Fig. 3) could occur even before the permanent deformation (or yielding) without showing any appreciable energy dissipation (Fig. 6). Such a disparity is most likely due to the differences in the test methodology. In this study we directly defined yielding at the strain level where the permanent deformation began with consideration of viscoelastic behavior during the loading process; whereas in the other studies yielding has been defined using 0.2% strain offset approach, which may overestimate the yield strength. Presently, there appears to be limited damage (small modulus loss) at the early stage of deformation that is not necessarily related to permanent deformation in bone, but instead may reflect the contribution of existing damage to the viscous behavior of bone tissue.

At Stage II, a sudden change in patterns for modulus loss and viscous responses of bone could be observed (Figs. 4 and 5), thus implying that some mechanistic changes governing the mechanical behavior of bone have occurred. In Stage I, 'fast' damage accumulation and increased involvement of collagen in load bearing seem to dominate the mechanical behavior of bone with limited energy dissipation. Contrarily, the major portion of energy dissipation in bone takes place in Stage II, with saturated viscous responses and limited modulus loss. Such changes suggest that damage accumulation and viscous behavior (*i.e.*, collagen involvement in load bearing) of bone are highly interrelated. This is in good agreement with the results reported in the literature.^{11,23,33,42,53-55} For example, previous studies have shown that there is a relationship between damage and the viscous-related properties of bone.^{11,33,53} More recently, inducing a flaw in bone was found to increase the energy dissipation by viscous means ($\tan \Delta$) as measured by dynamic mechanical analysis.⁵⁵ Thus, it is presumable that when the damage accumulation slows down significantly as strain crosses a threshold (about 1.0% for both age groups in this study), the contribution of collagen to load bearing would saturate accordingly. In other words, the viscous response of bone reaches an equilibrium state when a relatively constant portion of collagen is exposed to load bearing. Although the underlying mechanics for viscous behavior of collagen are still unclear, Sasaki and Enyo⁵⁶ (who fitted exponential decay models to the shear relaxation behavior of bovine bone samples) speculated that one cause of stress relaxation was the rearrangement of distorted collagen molecules under strain.

The energy dissipation in Stage II seems to increase linearly with increasing strain independent of the saturating modulus loss (damage accumulation) and viscous response (collagen involvement) of bone. Not surprisingly, the U_p increases because the plastic or permanent strain increases linearly with the applied strain to bone. However, further investigation is necessary to explain why the U_h and U_{er} continually increase with little changes in the viscoelastic response and damage accumulation in bone. Nonetheless, it could be speculated that the U_{er} likely results from the reversible interfacial deformation occurring between the mineral and collagen phase, whereas the increase in the U_h could be realized through the increased deformation rather than amount of the collagen phase exposed to the load bearing in bone.

One limitation to the present study is that the bone specimens are tested only in tension. In the other loading modes, the mechanical behavior of bone may be different.^{18,33,57} This information is important to fully understand the mechanical behavior of bone under more complex loading modes. To address this issue, further investigations are needed. Another limitation is that specimens were prepared solely from anterior quadrants of human tibia diaphyses along the longitudinal axis. Thus, the possible dependence of tissue properties on the location (anatomic aspects) and orientations were not taken into account in this study. In fact, the tissue properties may be significantly affected by these factors.^{16,58}

In summary, the results of the present study indicate that the mechanical behavior of bone as a function of progressive deformation consists of two successive stages: 1) acute damage accumulation (or modulus loss) and sharply increased viscous response ($\Delta\sigma$ and τ) with limited energy dissipation up to 1.0% strain; 2) slow damage accumulation and saturated viscous response with major energy dissipation in the successive deformation beyond 1.0% strain. Although unknown, it is conceivable that mechanistic changes in bone ultrastructure are involved in these distinct deformation stages. In addition, aging seems to have little effects on the mechanical behavior of bone except that elderly bone fails at much smaller strain compared with that of middle-aged bone, thereby giving rise to an age effect on the post-yield energy capacity of cortical bone.

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Figure 1.

Loading tensile bone specimens in a cyclic fashion (a typical stress-strain curve is shown in graph A) generates mechanical properties as a function of strain (an example of stress relaxation versus strain for each specimen indicating the donor's gender and age is shown in graph B). The long-short dashed line depicts a predicted stress-strain curve for a monotonic test that would 'envelop' the cycle behavior as suggested by Zioupos et al.⁴⁸ The vertical dashed line depicts a possible change in damaging mechanisms as the stress relaxation peaks at 1% strain. The vertical solid line indicates the point of yielding (shown for middle aged bone).

Figure 2.

Stress-strain relationship obtained at progressive strain levels is similar to a monotonic stress-strain curve. It is noteworthy that the middle aged yield strain (ϵ_y) derived from permanent strain criteria corresponds to the beginning of non-linearity, and the transition strain derived from peak stress relaxation corresponds to the end of non-linearity.

Figure 3.

The permanent (plastic) strain becomes appreciable in excess of 0.43% strain, and increases almost linearly with increasing strain. Both middle-aged and elderly bone specimens behave in a similar manner except the elderly bone has a lower yield strain (Table 4) and fails prematurely.

Figure 4.

The modulus loss experiences two stages of changes: a sharp drop in the early deformation after yielding, and then after the transition, the rate in change decreases with increasing strain. The modulus loss for both middle-aged and elderly bone appears to be similar except for the premature failure of the elderly bone.

Figure 5.

Time constant of stress relaxation (τ_i) is highly variable before yielding, decreases after yielding, and plateaus after the transition. The viscous behavior for both middle-aged and elderly bone seems to be similar except for the premature failure of the elderly bone.

Figure 6.

Energy dissipation as a function of applied strain in the three pathways: a) plastic strain energy dissipation; b) elastic release strain energy dissipation; and c) hysteresis energy dissipation. With the majority of dissipation occurring after the transition, the behavior for both middle-aged and elderly bone seems to be similar until the premature failure of the elderly bone.

Table 1

A number of age-related changes in bone at different length scales have been associated with changes in bone quality.

Length Scale	Age-related Effect		Mechanical Property		Reference
Bulk mm	Mineral density	↓	Strength	↓	Smith and Smith ⁵⁹
Bulk mm	Hypermineralization	↑	Impact strength	↓	Currey et al. ³⁰
100 µm	Osteons per area	↑	Tensile strength	↓	Evans ⁶⁰
100 µm	Percentage osteons	↑	Resistance to crack propagation	↓	Yeni et al. ⁶¹
10-50 µm	Porosity	↑	Post-yield toughness	↓	McCalden et al. ¹
10-50 µm	Porosity	↑	Resistance to crack propagation	↓	Yeni et al. ⁶²
1-5 µm	Microdamage	↑	Work-to-fracture	↓	Zioupou ⁶³
1-5 µm	Microdamage	↑	Resistance to crack propagation	↓	Norman et al. ¹⁵
100 nm	Collagen shrinkage temperature	↓	Toughness	↓	Zioupou et al. ⁴
100 nm	Non-enzymatic crosslinks (pentosidine)	↑	Fracture toughness	↓	Wang et al. ³

Table 2

The numbers of specimens are given for each range of strain in which statistical analyses were performed to test for an age effect on the mechanical properties of bone.

Strain range	Deformation stage	Middle aged	Elderly
0.0030 – 0.0043	Pre-yield	n = 9	n = 8
0.0060 – 0.0084	Stage I	n = 8	n = 6
0.0090 – 0.0120	Transition	n = 8	n = 6
0.0140 – 0.0190	Early Stage II	n = 9	n = 6

Table 3

p-values from the statistical analyses indicate that most properties do not differ between middle and old aged bone within all deformation regions.

Property	Symbol	Pre-yield	Stage I	Transition	Early Stage II
Strain ^a	ϵ_i	0.8612	0.6074	0.7031	0.7725
Permanent strain	$\epsilon_{p,i}$	0.3102	0.1920	0.4753	0.3121
Stress relaxation	$\Delta\sigma_i$	0.0958	0.1789	0.3193	0.3232
Time constant	τ_i	0.4989	0.2707	0.1371	0.0279
Modulus	E_i	0.2962	0.1242	0.2108	0.1057
Maximum stress	$\sigma_{\max,i}$	0.1479	0.1682	0.0845	0.0804
Plastic strain energy	$U_{p,i}$	0.1476	0.2489	0.3021	0.1669
Elastic release strain energy	$U_{er,i}$	0.1398	0.2986	0.2514	0.3745
Hysteresis energy	$U_{h,i}$	0.1004	0.2835	0.3104	0.4087

^a p-values for strain are from a two-sided hypothesis test checking for consistency, while p-values from all other properties are from one-sided hypothesis test testing for greater than or less than.

Table 4

There are significant age-related differences in the mechanical properties of bone when properties are calculated for the final cycle (subscript f) before failure.

Property	Unit	Middle aged (n=9)	Elderly (n=8)	p-value
ε_y^a	mm/mm	0.0043 ± 0.0002	0.0039 ± 0.0003	0.0036
ε_T	mm/mm	0.0100 ± 0.0011	0.0101 ± 0.0023	0.4268
ε_f^b	mm/mm	0.0285 ± 0.0065	0.0153 ± 0.0029	<0.0001
$\varepsilon_{p,f}$	mm/mm	0.0091 ± 0.0021	0.0043 ± 0.0010	<0.0001
$\Delta\sigma_T$	%	16.3 ± 1.2	16.4 ± 1.3	0.4612
$\Delta\sigma_f$	%	13.3 ± 1.1	15.2 ± 1.8	0.0073
τ_f	sec.	7.03 ± 0.36	6.17 ± 0.76	0.0027
E_f	GPa	4.84 ± 1.04	7.61 ± 1.51	0.0001
$\sigma_{\max,f}$	MPa	104.9 ± 8.2	96.8 ± 6.2	0.0177
$U_{p,f}$	MJ/m ³	0.858 ± 0.208	0.351 ± 0.086	<0.0001
$U_{er,f}$	MJ/m ³	0.498 ± 0.166	0.194 ± 0.059	0.0001
$U_{h,f}$	MJ/m ³	0.507 ± 0.161	0.225 ± 0.052	0.0002

^a Properties independent of cycle: ε_y -yield strain, ε_T -transition strain, and $\Delta\sigma_T$ -peak stress relaxation.

^b Properties of the last cycle: ε_f -maximum strain, $\varepsilon_{p,f}$ -maximum plastic strain, $\Delta\sigma_f$ -stress relaxation, τ_f -time constant, E_f -final elastic modulus, $\sigma_{\max,f}$ -strength, $U_{p,f}$ -maximum plastic strain energy, $U_{er,f}$ -maximum elastic release strain energy, and $U_{h,f}$ -maximum hysteresis energy.