Published in final edited form as:

J Biomech. 2009 February 9; 42(3): 202–209. doi:10.1016/j.jbiomech.2008.10.022.

Probabilistic Failure Analysis of Bone Using a Finite Element Model of Mineral-Collagen Composites

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Abstract

Microdamage accumulation is a major pathway for energy dissipation during the post-yield deformation of bone. In this study, a two-dimensional probabilistic finite element model of a mineral-collagen composite was developed to investigate the influence of the tissue and ultrastructural properties of bone on the evolution of microdamage from an initial defect in tension. The probabilistic failure analyses indicated that the microdamage progression would be along the plane of the initial defect when the debonding at mineral-collagen interfaces was either absent or limited in the vicinity of the defect. In this case, the formation of a linear microcrack would be facilitated. However, the microdamage progression would be scattered away from the initial defect plane if interfacial debonding takes place at a large scale. This would suggest the possible formation of diffuse damage. In addition to interfacial debonding, the sensitivity analyses indicated that the microdamage progression was also dependent on the other material and ultrastructural properties of bone. The intensity of stress concentration accompanied with microdamage progression was more sensitive to the elastic modulus of the mineral phase and the nonlinearity of the collagen phase, whereas the scattering of failure location was largely dependent on the mineral to collagen ratio and the nonlinearity of the collagen phase. The findings of this study may help understanding the post-yield behavior of bone at the ultrastructural level and shed light on the underlying mechanism of bone fractures.

Keywords

Bone; Microdamage; Probabilistic failure mechanics; Finite element analysis; Mineral-collagen composites

1. Introduction

It has been commonly accepted that deterioration in bone quality is a major reason for age-related bone fractures due to the reduced toughness of the tissue (Schaffler et al., 1995; Burr et al., 1997). Bone toughness, as the total energy required to produce complete fracture, is determined mostly by its post-yield behavior (Currey, 2001), which is characterized by a marked microdamage accumulation (Ziopoulos et al., 1994; Reilly and Currey, 1999; Vashishth

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et al., 2000). Two major types of microdamage have been observed in bone tissues: linear microcrack and diffuse damage. Linear microcracks are individual cracks at a size of microns or larger (Schaffler et al., 1994; Burr et al., 1997) whereas diffuse damage is a damage zone that consists of an extensive network of fine, ultrastructural-level defects (Schaffler et al., 1995; Boyce et al., 1998; Fazzalari et al., 1998; Fazzalari et al., 1998; Vashishth et al., 2000). Microdamage formation serves as a toughening mechanism for bone tissues and plays an important role in dissipating energy (Vashishth et al., 2000; Vashishth et al., 2003).

A number of experimental and theoretical studies have been performed to study the failure behavior of bone at the bulk level (Carter and Caler, 1985; Krajcinovic et al., 1987; Fondrk et al., 1988; Guo et al., 1994; Pattin et al., 1996; Griffin et al., 1997; Levenston and Carter, 1998; Pidaparti et al., 2001). Among these studies, modulus degradation of bone samples has been investigated using continuum damage theory or determined experimentally for a variety of loading modes: tension, compression and bending. In addition, both linear and nonlinear elastic fracture mechanics have been used to study the initiation and propagation of cracks in bone (Norman et al., 1996; Norman and Wang, 1997; Vashishth et al., 1997; Guo et al., 1998; Taylor, 1998; Vashishth et al., 2000; Yeni and Norman, 2000; Malik et al., 2003; Vashishth et al., 2003; Nalla et al., 2005; Ritchie et al., 2005; Gao, 2006; Ritchie et al., 2006; Yang et al., 2006). However, the bulk failure behavior of bone is actually a manifestation of failure mechanisms at different hierarchical levels of the tissue (*e.g.*, lamella, osteon, cement line, interstitial tissue, etc.). Thus, it becomes necessary to understand the failure behavior of bone at all hierarchical levels in order to elucidate the failure mechanism of the tissue.

In this study, a probabilistic failure analysis approach was developed to investigate the mechanism of microdamage progression in lamellar structures, which are the basic building block for both human trabecular and cortical bone tissues and can be modeled as a mineral-collagen composite. From the perspective of composite materials, the failure mechanism of a composite is determined by the material and structural properties of its components and their interactions. The hypothesis of this study was that the interfacial debonding between collagen fibrils and the mineral phase may play a significant role in microdamage progression in bone.

2. Methods

2.1 Overall procedures

Since bone is inhomogeneous in nature, probabilistic failure analyses were performed to predict the failure behavior in lamellar structures. Briefly, a two-dimensional plane-strain finite element (FEM) model of mineral-collagen composites was first developed (Figure 1). Then, Monte Carlo techniques were used to randomly designate material and structural properties (*i.e.*, random variables) to the model to create multiple samples for probabilistic analyses with a required power. In addition, a strength value was generated randomly using Monte Carlo techniques for each element in each sample of the model (*i.e.*, random fields). All the samples were subjected to a constant displacement load. Failure of an element would be considered when the stress at its centroid exceeds its strength. The probability of failure of each element was calculated from all samples and the failure location was defined at the element with maximum failure probability. By introducing a new defect at the predicted failure location, a new finite element model was subsequently established to predict the next failure location. By repeating the procedure, the pattern of damage progression in the tissue was investigated. Finally, the sensitivity measures of microdamage formation to the material and ultrastructural properties of bone were also investigated.

2.2 Finite element models

Finite element analysis was conducted using a general purpose finite element software package ABAQUS (SIMULIA, Providence, Rhode Island). The model contained alternating layers of mineral and collagen phases to represent the mineral-collagen composite in bone lamellae and was subjected to a tensile load along the longitudinal direction (Figure 1). An initial defect was introduced as a discontinuity with a width of half the thickness of the mineral layer (Figure 1). It was assumed that the mineral phase fails first because it carries the most of load and has a failure strain at least two orders of magnitude less than that of collagen fibrils (Puxkandl et al., 2002). The interface between collagen and mineral phases was assumed to be perfectly bonded except in the vicinity of the initial defect, whose integrity was specifically designated as perfect or debonded during the analysis (Figure 1). The interfacial debonding was modeled as an interfacial crack with a length of L between the mineral and the adjacent collagen layers. The results of our preliminary study indicated that singularity at interfacial crack tips affected the stress distribution only at the vicinity of the tips, with little differences in the other regions being observed between the models with and without the singularity elements. Since incorporating singularity into the model was time-consuming and would increase the computing cost, the singularity element was not used in this study for simplicity while without losing reasonable accuracy. All dimensions in the model were normalized against the diameter of collagen fibrils, which was approximated as about 54 nm (Cassella et al., 1994; Sarathchandra et al., 1999).

Constitutive laws for mineral and collagen phases in the mineral-collagen composite were as follows: isotropic linear elastic behavior for the mineral phase ($E_m = 125$ GPa, and $\nu_m = 0.3$) (Katz and Ukraincik, 1971); and a nonlinear elastic behavior obeying a power law (Wang and Qian, 2006) for the collagen phase:

$$\sigma = E_c \varepsilon^n \quad (1)$$

where E_c is the stiffness factor, n is the nonlinearity of collagen fibrils, σ is nominal stress and ε is nominal strain. The Poisson's ratio of the collagen phase (ν_c) was chosen as 0.35 (Katz, 1971). The nonlinear constitutive law of collagen was implemented in ABAQUS by using the Ogden strain energy potential to represent the hyper-elastic behavior of collagen (Zobitz et al., 2001). Uniaxial tensile test data of collagen were used to obtain the parameters required for determining the strain energy potential.

The finite element models were meshed using 4-node quadrilateral elements with reduced integration. A graded mesh was generated in the model with a refined mesh near the region of interest (*i.e.*, around defects) and a coarse mesh outside the region. A convergence study was carried out to determine the optimum mesh density of the model such that the peak stress in the model reached a consistent value. The mesh size in the region of interest was about a quarter of collagen thickness (13 nm) in both horizontal and vertical directions. Outside the region, the mesh size was 13 nm in the vertical direction, but varied from 90 nm to 900 nm in the horizontal direction. For a mineral-collagen composite with an initial defect, the total number of elements was 13,726. In addition, the number and length of collagen and mineral layers was increased during simulations whenever it was required to elude boundary effects.

2.3 Probabilistic failure analysis

2.3.1 Monte Carlo simulations—In this study, the required number of samples ($N=200$) for Monte Carlo simulations was determined by preliminary studies to ensure that the percentage error in the calculated probability of failure from the true probability of failure was within a desired level (14% in this study) (Millwater and Wirsching, 2003). For each of these

samples, a random set of material and ultrastructural properties was assigned based on their probability distributions indicated in Table 1 (see Appendix I). In addition, the strength distribution in each sample was defined using a random field approach (see Appendix II). The generation of values for random variables and random fields was implemented using a commercial probabilistic software NESSUS (Southwest Research Institute, San Antonio, TX).

2.3.2 Response models—Since the failure behavior of the mineral phase is brittle in nature, the maximum principal stress (σ_{max}) was used as the failure criterion. σ_{max} of each element in the finite element models was calculated using ABAQUS and expressed as a response model,

$$\sigma_{max} = f_e(E_m, E_c, n, R, L) \quad (2)$$

where E_m , E_c , n , R , L are material and structural properties of bone constituents as defined earlier. The probabilistic software NESSUS was used to assist ABAQUS in running the finite element models with the material and structural parameters generated by Monte Carlo sampling techniques.

2.3.3 Failure criterion of elements—The failure criterion for each element was defined as:

$$g_i = \sigma_{strength} - \sigma_{max} \quad (3)$$

where g_i is a parameter used as a failure index, $\sigma_{strength}$ is the strength of the element defined by a random field (see Appendix II and Figure 2), and σ_{max} is the maximum principal stress in the element determined by the finite element model. Failure occurs when g_i is less than or equal to zero, whereas no failure occurs if g_i is greater than zero.

2.3.4 Determination of failure location in each model—For each model, the probability of failure in each element was determined by comparing the number of samples with predicted failures at this particular element to the total number of samples analyzed. The failure location for the model was then defined at the element with the maximum failure probability.

2.3.5 Microdamage progression—As additional defects were continually introduced into the mineral-collagen composite, the pattern of damage progression could be eventually observed. A Python script (Python Software Foundation, Hampton, NH) was written to automatically track the damage progression in the mineral-collagen composite.

2.4 Interfacial debonding length

Interfacial debonding was introduced around the defects and its length (L) was varied from 1 to 20 times of the thickness of collagen layers. By doing so, changes of microdamage progression with interfacial debonding length could be investigated. This information is very important to predict the effect of interfacial integrity between the mineral and collagen phases on the microdamage progression in bone. In this study, damage scattering with respect to each interfacial debonding length was calculated as the average distance between adjacent defects in the models.

2.5 Sensitivity analysis

Sensitivity measures give the relative importance of individual random variables and their statistics on the probable occurrence of specific events (see Appendix III). In this study, the sensitivity measures were based on the mean and the standard deviation of the input random variables. Changes in the failure location and the intensity of stress concentration (*i.e.*, peak stress in the model) were investigated as a function of the variability of the material and structural properties of mineral and collagen phases.

3. Results

3.1 Probabilistic failure prediction

Stress concentrations were observed at the immediately neighboring mineral layers above and below the initial defect (Figure 3). Without interfacial debonding, the stress concentration region was narrow and immediately above or below the initial defect (Figure 3a), whereas the stress concentration region expanded significantly when interfacial debonding was present, (Figure 3b). Largely due to such changes in stress concentration, probabilistic failure analyses also demonstrated that the pattern of microdamage progression depended on whether interfacial debonding was present in the mineral-collagen composite. For instance, the predicted failure location in the model without interfacial debonding was immediately below the initial defect in the adjacent mineral layers (Figure 4a). In contrast, the predicted failure location in the model with interfacial debonding deviated away from the initial defect (Figure 4b).

As the number of defects increased with the simulation, the pattern of microdamage progression became more obvious. Without interfacial debonding, microdamage progression proceeded along the plane of the initial defect (Figure 5a). With interfacial debonding, the microdamage progression was scattered away from the initial defect (Figure 5b).

3.2 The effect of interfacial debonding length

The pattern of microdamage progression exhibited its dependency on the interfacial debonding length (Figure 6), showing that there were three regions in the plot of damage scattering vs. interfacial debonding length. In the region I, the interfacial debonding length was at a small scale ($L \leq 5$) and the damage scattering was close to zero. Region II was a transition region ($5 < L < 7$) in which damage scattering increased acutely. In the region III, the interfacial debonding length was at a large scale ($L \geq 7$) and the damage scattering increased proportionally with the interfacial debonding length. This may suggest that there is a critical interfacial debonding length that determines whether the damage progression is in a linear or a scattered manner.

3.3 Sensitivity measures of material and structural parameters

The occurrence of damage progression in bone was more sensitive to the mean rather than the standard deviation of material and structural parameters (Figure 7). The sensitivity analyses indicated that the predicted failure location was sensitive to the interfacial debonding length, the mineral to collagen thickness ratio, and the nonlinearity of collagen phase (Figure 7a). The interfacial debonding length had the greatest effect, followed by the mineral to collagen thickness ratio and nonlinearity of the collagen phase. Increasing the interfacial debonding length and nonlinearity of collagen phase caused the failure location to move away from the initial defect. On the contrary, increasing the mineral to collagen thickness ratio caused the failure location to move towards the initial defect.

In addition, the sensitivity analyses indicated that the intensity of stress concentration (*i.e.*, the peak stress in the model) induced by damage formation was more sensitive to the modulus of the mineral phase and the nonlinearity of the collagen phase than the other material and

structural parameters (Figure 7b). Mineral modulus had a positive effect on the stress concentration, whereas the nonlinearity of the collagen phase had a negative effect.

4. Discussion

The simulation of microdamage progression in a mineral-collagen composite model with an initial defect was performed in this study. Depending on whether or not interfacial debonding is present around defects, the outcome of microdamage progression in bone is significantly different. Without interfacial debonding, the stress concentration in the adjacent mineral phase exhibits a narrow region with respect to the initial defect plane (Figure 3a). Such a narrow zone of stress concentration would significantly increase the probability of failure in the mineral layers immediately above or below the initial defect. This would facilitate a series failure of mineral layers along the initial defect plane, and subsequently develop into a linear microcrack by coalescence of these defects (Figure 4a and Figure 5a).

However, interfacial debonding between the mineral and collagen phases may result in a large expansion of stress concentration zones that could be observed in the adjacent mineral layers (Figure 3b), thus increasing the probability of failure at a location that deviates from the plane of the initial defect. This would allow for scattering of microdamage formation around the initial defects, and favor the formation of diffuse damage (Figure 4b and Figure 5b).

Material and ultrastructural properties may also have effects on microdamage progression in bone. The sensitivity analyses of this study indicate that the failure location is most sensitive to the debonding length at mineral-collagen interfaces. The longer is the debonding length at the interfaces, the farther away the failure location would deviate from the plane of the initial defect, thus increasing the chance to form scattered (diffuse) damage (Figure 4b and Figure 5b). These results may help understand the contribution of the mineral-collagen interface to the mechanical behavior of bone. Walsh et al. reported that altering interfacial bonding between the mineral and collagen with varied ionic strength solutions may lead to deterioration of mechanical properties of bone (Walsh and Guzelsu, 1993; Walsh and Guzelsu, 1994; Walsh et al., 1994). In addition, based on the measurements using a synchrotron x-ray scattering technique, Gupta et al. postulated that matrix shearing flow between mineralized collagen fibrils plays a significant role in the post-yield deformation of bone (Gupta et al., 2005). Nonetheless, the underlying mechanism is still unclear. To our knowledge, this study is the first attempt to mechanistically investigate the involvement of mineral-collagen interfaces in the mechanical behavior of bone.

The results of this study also indicate that the intensity of stress concentration (peak stress) induced by damage formation in the mineral-collagen composite is most sensitive to the elastic modulus of the mineral phase and the nonlinearity of the collagen phase. A high elastic modulus of the mineral phase and a decreased nonlinearity of the collagen phase would lead to an increased peak stress, which would increase the failure probability of the tissue. Previous studies have shown that hypermineralized bone tissues behave more brittle than normal tissues (Boyce and Bloebaum, 1993; Vajda and Bloebaum, 1999). Since the elastic modulus of the mineral phase is directly related to the mineralization of the tissue, the high peak stress predicted by this model due to elevated mineral modulus may be one of the reasons for the brittleness of hypermineralized bone tissues. Although little information is available in the literature regarding the effect of collagen nonlinearity on the mechanical behavior of bone, a study by Vashishth et al. reported that an increased stiffness of the collagen phase by non enzymatic crosslinking is associated with an increase in the yield strength of the tissue (Vashishth et al., 2001), which may be caused by the decreasing nonlinearity of the collagen phase.

The present study has some limitations. First, for simplicity alternating layers of collagen and mineral phases were used to simulate the behavior of bone. However, a staggered model of mineralized collagen fibrils (Fratzl et al., 1993; Jager and Fratzl, 2000) can better represent the properties of the collagen phase in our model and may shed more insight on the simulation of the microdamage accumulation. Second, the interfacial debonding was modeled as a complete separation between the mineral and collagen phases. In reality, cohesive behavior may still exist at the damaged interfaces between the mineral and collagen phases, thereby affecting the microdamage progression in bone. Thus, use of cohesive elements may allow for modeling such a behavior and to investigate its contribution to the microdamage progression.

5. Conclusion

The probabilistic failure analyses of this study demonstrated that the presence of interfacial debonding around an initial defect plays a significant role in microdamage progression in a mineral-collagen composite. Secondary to interfacial debonding, other material and ultrastructural properties of bone constituents may also affect the damage scattering and the intensity of stress concentration in the tissue.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was supported by an NIH/NIA grant (AG027780). We are grateful to Mr. Daniel Sparkman for his help in data processing.

References

- Arsenault AL. A comparative electron microscopic study of apatite crystals in collagen fibrils of rat bone, dentin and calcified turkey leg tendons. *Bone Miner* 1989;6:165–77. [PubMed: 2765707]
- Arsenault AL. Image analysis of mineralized and non-mineralized type I collagen fibrils. *J Electron Microscop Tech* 1991;18:262–8. [PubMed: 1880599]
- Boyce TM, Bloebaum RD. Cortical aging differences and fracture implications for the human femoral neck. *Bone* 1993;14:769–78. [PubMed: 8268051]
- Boyce TM, Fyhrie DP, Glotkowski MC, Radin EL, Schaffler MB. Damage type and strain mode associations in human compact bone bending fatigue. *Journal of Orthopaedic Research* 1998;16:322–9. [PubMed: 9671927]
- Burr DB, Forwood MR, Fyhrie DP, Martin RB, Schaffler MB, Turner CH. Bone microdamage and skeletal fragility in osteoporotic and stress fractures. *Journal of Bone & Mineral Research* 1997;12:6–15. [PubMed: 9240720]
- Carter DR, Caler WE. A cumulative damage model for bone fracture. *Journal of Orthopaedic Research* 1985;3:84–90. [PubMed: 3981298]
- Cassella JP, Barber P, Catterall AC, Ali SY. A morphometric analysis of osteoid collagen fibril diameter in osteogenesis imperfecta. *Bone* 1994;15:329–34. [PubMed: 8068454]
- Currey J. Sacrificial bonds heal bone. *Nature* 2001;414:699. [PubMed: 11742376]
- Elliott SR, Robinson RA. The water content of bone. I. The mass of water, inorganic crystals, organic matrix, and CO₂ space components in a unit volume of the dog bone. *J Bone Joint Surg Am* 1957;39-A:167–88. [PubMed: 13385272]
- Fazzalari NL, Forwood MR, Manthey BA, Smith K, Kolesik P. Three-dimensional confocal images of microdamage in cancellous bone. *Bone* 1998;23:373–8. [PubMed: 9763150]
- Fazzalari NL, Forwood MR, Smith K, Manthey BA, Herreen P. Assessment of cancellous bone quality in severe osteoarthritis: bone mineral density, mechanics, and microdamage. *Bone* 1998;22:381–8. [PubMed: 9556139]

- Fondrk M, Bahniuk E, Davy DT, Michaels C. Some viscoplastic characteristics of bovine and human cortical bone. *J Biomech* 1988;21:623–30. [PubMed: 3170617]
- Fratzl P, Fratzl-Zelman N, Klaushofer K. Collagen packing and mineralization. An x-ray scattering investigation of turkey leg tendon. *Biophys J* 1993;64:260–6. [PubMed: 8431546]
- Gao H. Application of fracture mechanics concepts to hierarchical biomechanics of bone and bone-like materials. *International Journal of Fracture* 2006;138:101–137.
- Gardner TN, Elliott JC, Sklar Z, Briggs GA. Acoustic microscope study of the elastic properties of fluorapatite and hydroxyapatite, tooth enamel and bone. *J Biomech* 1992;25:1265–77. [PubMed: 1328251]
- Griffin LV, Gibeling JC, Martin RB, Gibson VA, Stover SM. Model of flexural fatigue damage accumulation for cortical bone. *J Orthop Res* 1997;15:607–14. [PubMed: 9379272]
- Guo XE, Liang LC, Goldstein SA. Micromechanics of osteonal cortical bone fracture. *Journal of Biomechanical Engineering* 1998;120:112–7. [PubMed: 9675689]
- Guo XE, McMahon TA, Keaveny TM, Hayes WC, Gibson LJ. Finite element modeling of damage accumulation in trabecular bone under cyclic loading. *J Biomech* 1994;27:145–55. [PubMed: 8132682]
- Gupta HS, Wagermaier W, Zickler GA, Raz-Ben Aroush D, Funari SS, Roschger P, Wagner HD, Fratzl P. Nanoscale deformation mechanisms in bone. *Nano Lett* 2005;5:2108–11. [PubMed: 16218747]
- Haldar, A.; Mahadevan, S. Probability, reliability and statistical methods in engineering design. John Wiley & Sons; 2000.
- Huja SS, Beck FM, Thurman DT. Indentation properties of young and old osteons. *Calcif Tissue Int* 2006;78:392–7. [PubMed: 16830198]
- Jager I, Fratzl P. Mineralized collagen fibrils: a mechanical model with a staggered arrangement of mineral particles. *Biophys J* 2000;79:1737–46. [PubMed: 11023882]
- Katz JL. Hard tissue as a composite material. I. Bounds on the elastic behavior. *Journal of Biomechanics* 1971;4:455–73. [PubMed: 5133361]
- Katz JL, Ukraincik K. On the anisotropic elastic properties of hydroxyapatite. *J Biomech* 1971;4:221–7. [PubMed: 5119417]
- Kinney JH, Habelitz S, Marshall SJ, Marshall GW. The importance of intrafibrillar mineralization of collagen on the mechanical properties of dentin. *J Dent Res* 2003;82:957–61. [PubMed: 14630894]
- Krajcinovic D, Trafimow J, Sumarac D. Simple constitutive model for a cortical bone. *J Biomech* 1987;20:779–84. [PubMed: 3654677]
- Levenston ME, Carter DR. An energy dissipation-based model for damage stimulated bone adaptation. *Journal of Biomechanics* 1998;31:579–86. [PubMed: 9796679]
- Malik CL, Stover SM, Martin RB, Gibeling JC. Equine cortical bone exhibits rising R-curve fracture mechanics. *J Biomech* 2003;36:191–8. [PubMed: 12547356]
- Martin, RB.; Burr, DB.; Sharkey, NA. Skeletal tissue mechanics. New York: Springer; 1998.
- Millwater, HR.; Wirsching, P. ASM Handbook: Volume 11, Failure Analysis and Prevention. Materials Park, OH: ASM International; 2003. Analysis method for probabilistic life assessment; p. 250-268.
- Nalla RK, Kruzic JJ, Kinney JH, Ritchie RO. Mechanistic aspects of fracture and R-curve behavior in human cortical bone. *Biomaterials* 2005;26:217–31. [PubMed: 15207469]
- Norman TL, Nivargikar SV, Burr DB. Resistance to crack growth in human cortical bone is greater in shear than in tension. *Journal of Biomechanics* 1996;29:1023–31. [PubMed: 8817369]
- Norman TL, Wang Z. Microdamage of human cortical bone: incidence and morphology in long bones. *Bone* 1997;20:375–9. [PubMed: 9108359]
- Olde Damink LH, Dijkstra PJ, Van Luyn MJ, Van Wachem PB, Nieuwenhuis P, Feijen J. Changes in the mechanical properties of dermal sheep collagen during in vitro degradation. *J Biomed Mater Res* 1995;29:139–47. [PubMed: 7738060]
- Pattin CA, Caler WE, Carter DR. Cyclic mechanical property degradation during fatigue loading of cortical bone. *Journal of Biomechanics* 1996;29:69–79. [PubMed: 8839019]
- Pidaparti RM, Wang QY, Burr DB. Modeling fatigue damage evolution in bone. *Biomed Mater Eng* 2001;11:69–78. [PubMed: 11352114]

- Puxkandl R, Zizak I, Paris O, Keckes J, Tesch W, Bernstorff S, Purslow P, Fratzl P. Viscoelastic properties of collagen: synchrotron radiation investigations and structural model. *Philos Trans R Soc Lond B Biol Sci* 2002;357:191–7. [PubMed: 11911776]
- Reilly GC, Currey JD. The development of microcracking and failure in bone depends on the loading mode to which it is adapted. *J Exp Biol* 1999;202:543–52. [PubMed: 9929457]
- Ritchie RO, Kinney JH, Kruzic JJ, Nalla RK. A fracture mechanics and mechanistic approach to the failure of cortical bone. *Fatigue and Fracture of Engineering Materials and Structures* 2005;28:345–371.
- Ritchie RO, Nalla RK, Kruzic JJ, Ager III, Balooch G, Kinney JH. Fracture and ageing in bone: Toughness and structural characterization. *Strain* 2006;42:225–232.
- Robinson RA. An electron-microscopic study of the crystalline inorganic component of bone and its relationship to the organic matrix. *J Bone Joint Surg Am* 1952;34-A:389–435. [PubMed: 14917711]
- Robinson RA, Watson ML. Collagen-crystal relationships in bone as seen in the electron microscope. *Anat Rec* 1952;114:383–409. [PubMed: 12996880]
- Roschger P, Paschalis EP, Fratzl P, Klaushofer K. Bone mineralization density distribution in health and disease. *Bone* 2008;42:456–66. [PubMed: 18096457]
- Ruffoni D, Fratzl P, Roschger P, Klaushofer K, Weinkamer R. The bone mineralization density distribution as a fingerprint of the mineralization process. *Bone* 2007;40:1308–19. [PubMed: 17337263]
- Sarathchandra P, Pope FM, Ali SY. Morphometric analysis of type I collagen fibrils in the osteoid of osteogenesis imperfecta. *Calcif Tissue Int* 1999;65:390–5. [PubMed: 10541766]
- Schaffler MB, Choi K, Milgrom C. Aging and matrix microdamage accumulation in human compact bone. *Bone* 1995;17:521–25. [PubMed: 8835305]
- Schaffler MB, Pitchford WC, Choi K, Riddle JM. Examination of compact bone microdamage using back-scattered electron microscopy. *Bone* 1994;15:483–8. [PubMed: 7526878]
- Taylor D. Microcrack growth parameters for compact bone deduced from stiffness variations. *J Biomech* 1998;31:587–92. [PubMed: 9796680]
- Vajda EG, Bloebaum RD. Age-related hypermineralization in the female proximal human femur. *Anatomical Record* 1999;255:202–11. [PubMed: 10359521]
- Vanmarcke, M. Random fields: analysis and synthesis. Cambridge, Massachusetts: The MIT Press; 1983.
- Vashishth D, Behiri JC, Bonfield W. Crack growth resistance in cortical bone: concept of microcrack toughening. *J Biomech* 1997;30:763–9. [PubMed: 9239560]
- Vashishth D, Gibson GJ, Khoury JI, Schaffler MB, Kimura J, Fyhrie DP. Influence of nonenzymatic glycation on biomechanical properties of cortical bone. *Bone* 2001;28:195–201. [PubMed: 11182378]
- Vashishth D, Koontz J, Qiu SJ, Lundin-Cannon D, Yeni YN, Schaffler MB, Fyhrie DP. In vivo diffuse damage in human vertebral trabecular bone. *Bone* 2000;26:147–52. [PubMed: 10678409]
- Vashishth D, Tanner KE, Bonfield W. Contribution, development and morphology of microcracking in cortical bone during crack propagation. *Journal of Biomechanics* 2000;33:1169–1174. [PubMed: 10854892]
- Vashishth D, Tanner KE, Bonfield W. Experimental validation of a microcracking-based toughening mechanism for cortical bone. *J Biomech* 2003;36:121–4. [PubMed: 12485646]
- Walsh WR, Guzelsu N. The role of ions and mineral-organic interfacial bonding on the compressive properties of cortical bone. *Biomed Mater Eng* 1993;3:75–84. [PubMed: 8369729]
- Walsh WR, Guzelsu N. Compressive properties of cortical bone: mineral-organic interfacial bonding. *Biomaterials* 1994;15:137–45. [PubMed: 8011860]
- Walsh WR, Labrador DP, Kim HD, Guzelsu N. The effect of in vitro fluoride ion treatment on the ultrasonic properties of cortical bone. *Ann Biomed Eng* 1994;22:404–15. [PubMed: 7998686]
- Wang X, Qian C. Prediction of microdamage formation using a mineral-collagen composite model of bone. *J Biomech* 2006;39:595–602. [PubMed: 16439230]
- Wu YT. Computational methods for efficient structural reliability and reliability sensitivity analysis. *AIAA Journal* 1994;32:1717–1732.

- Yang QD, Cox BN, Nalla RK, Ritchie RO. Fracture length scales in human cortical bone: The necessity of nonlinear fracture models. *Biomaterials* 2006;27:2095–2113. [PubMed: 16271757]
- Yeni YN, Norman TL. Calculation of porosity and osteonal cement line effects on the effective fracture toughness of cortical bone in longitudinal crack growth. *Journal of Biomedical Materials Research* 2000;51:504–9. [PubMed: 10880095]
- Zioupos P, Currey JD, Sedman AJ. An examination of the micromechanics of failure of bone and antler by acoustic emission tests and Laser Scanning Confocal Microscopy. *Medical Engineering & Physics* 1994;16:203–12. [PubMed: 8061906]
- Ziv V, Wagner HD, Weiner S. Microstructure-microhardness relations in parallel-fibered and lamellar bone. *Bone* 1996;18:417–28. [PubMed: 8739899]
- Zobitz ME, Luo ZP, An KN. Determination of the compressive material properties of the supraspinatus tendon. *J Biomech Eng* 2001;123:47–51. [PubMed: 11277301]

Figure 1.

Schematic illustration of finite element models for a mineral-collagen composite, which consists of alternate layers of mineral and collagen phases. The mineral-collagen composite was initially subjected to a displacement load of 0.1% tensile strain at the remote end of the model. An initial defect was present in the central mineral layer of the composite. Two cases were considered in this study: without (A) and with (B) interfacial debonding around the defect. Interfacial debonding was introduced at both upper and lower interfaces between the mineral and collagen layers.

Figure 2.

The strength distribution in the mineral-collagen composite as a random field. A region of interest was selected around the initial defect to reduce the computing time and costs. The region of interest was determined to be greater than the stress concentration region around the defect. Outside the region of interest (stress concentration region), mineral strength was modeled as a constant. Collagen strength was considered as a constant in the whole composite.

Figure 3.

Maximum principal stress distribution in the mineral-collagen composite without (a) and with (b) interfacial debonding. The stress in collagen layers was much less than that in mineral layers. Without interfacial debonding (a), stress concentrations were observed in the adjacent mineral layers in a narrow region around the initial defect. With interfacial debonding (b), the zone of stress concentrations in the adjacent mineral layers was expanded along the debonded interfaces.

Figure 4.

Failure probability distribution in the mineral-collagen composite without (a) and with (b) interfacial debonding. Without interfacial debonding, the most likely failure location was immediately below the initial defect, whereas with interfacial debonding the failure location moved far away from the plane of the initial defect.

Figure 5.

Predictions of microdamage progression for the model without (a) and with (b) interfacial debonding. The numbers indicated the sequence of damage progression. The contour plot was the distribution of the maximal principal stress in the mineral-collagen composite.

Figure 6.

The relationship between damage scattering and interfacial debonding length. Damage scattering is defined as the average distance between adjacent defects.

Figure 7. Sensitivity measures of failure location (a) and peak stress (b) to the mean and standard deviation (S.D.) of material and ultrastructural parameters.