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Microdamage and Osteocyte-Lacuna Strain in Bone: A Microstructural Finite Element Analysis

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Damage accumulation in living tissues occurs when the rate of damage formation is greater than the rate of damage repair. For very large increases in the loading rate of bones, this can result in "stress fractures" due to the growth and coalescence of fatigue related microdamage. At lower increases of loading rates, the damage accumulation process is halted because there is time for adaptive bone-remodeling to occur in response to the new load. However, it is not known if there is a relationship between microdamage and bone remodeling per se. One hypothesis for the control of bone remodeling is that osteocytes sense strains and mediate osteoblastic and osteoclastic activity. The purpose of this study was to investigate whether damage generates strains which may trigger bone remodeling. If this were true, then accumulative damage would cause adaptive bone remodeling. This study applies the methods of finite element analysis to determine the effect of observed damage mechanisms on the proposed sensors of remodeling in Haversian bone. Individual lamellae are modeled and osteocyte-lacunae are included in a generalized plane strain geometric representation. It is predicted that microdamage alters the local deformation behavior around lacunae, and that the changes increase as microdamage accumulates. Hence, if damage accumulates in a bone, it could be sensed as a change in strain at a microstructural level. The results give theoretical support to the experimental studies that have shown a correlation between microdamage and the initiation of resorption as a first step in bone remodeling.

Introduction

Ballet dancers and soldiers are among those who sometimes fracture their bones under cyclic loading whose amplitude, if statically applied, would be insufficient to cause failure. Increased loading rates of bones after successful total joint replacement can also cause this type of fracture (McElwaine and Sheehan, 1982). "Stress fractures"—as they are called in orthopaedics—result from an accumulation and eventual coalescence of microdamage in the bone cross-section. Damage accumulation occurs because the bone turnover rate (remodeling rate) is insufficient to mend the microdamage as it is formed. The remodeling process occurs by resorption of aged bone and subsequent filling of the resorbed space with new tissue which eventually mineralizes (Parfitt, 1984). In compact Haversian bone, the newly deposited tissue forms an osteon and the process is called osteonal remodeling. It has been proposed that repair by osteonal remodeling is not a hit-or-miss process, but rather that the presence of a crack stimulates the bone remodeling sequence (Martin and Burr, 1989) and evidence to support this hypothesis has been provided by experiments (Burr et al., 1985, Mori and Burr, 1993).

Despite the fact that a relationship between microdamage and adaptive bone-remodeling was only tentatively proposed, many theories of how damage could stimulate adaptive bone-remodeling have been reported. Radin (1972) proposed that trabeculae oriented at an angle to the local load would undergo excessive damage accumulation and would remodel into alignment to survive. Carter et al. (1987) proposed that microdamage, oc-

curing in a daily loading cycle, could be a bone maintenance stimulus. Frost (1986) proposed a descriptive theory of bone response to mechanical stress—the Mechanostat theory. According to this theory, there is a physiological strain range where bone remodeling is in equilibrium, determined by metabolic factors alone. The lower limit of this range is given by a "remodeling" minimum-effective-strain and the upper limit is given by a "modeling" minimum-effective-strain. Hence the processes operating at either end of the remodeling equilibrium zone are not necessarily just negative and positive manifestations of the same process but may be different processes of remodeling and modeling. "Remodeling" is the coupled process of bone resorption and formation. "Modeling" is new bone deposition (without prior resorption) or bone resorption (not followed by deposition). Frost suggested that these processes are stimulated if the rate of microdamage formation changes due to unphysiological strains. For such a theory to work, bone tissue would need to be able to sense microdamage as it happens.

Cowin and Van Buskirk (1979) developed a mathematical formalism to predict the time-course of bone adaptation by considering the potential for adaptation to be a function of the difference between an actual strain and a homeostatic strain. In a related approach, Huiskes et al. (1987) simulated bone adaptation using the change of strain energy density in the mineralized bone tissue as the stimulus. Prendergast and Taylor (1994) developed a model to predict the time-course of bone adaptation by proposing that a change in the homeostatically-accumulated microdamage is a stimulus for bone adaptation. In their model, a continuous repair process is included to ensure that damage does not accumulate to failure. The process of bone-remodeling itself, whereby bone mass is continuously resorbed and apposed in a state of dynamic equilibrium, is not

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UNIT OF BONE WITH A CERTAIN MASS AND MICRODAMAGE

Fig. 1 The bone mass and the extent of microdamage determine the structural behavior of the bone and thus the mechanical stimulus that generates the remodeling signal. The remodeling signal could cause an alteration in remodeling activity that will tend to re-attain both the homeostatic strain (strain equilibrium) and a physiologically acceptable amount of microdamage (damage equilibrium).

described explicitly by these models. They assume that remodeling equilibrium is maintained by an adequate level of the stimulus and adaptively remodeled by a deviation from this level. If the remodeling equilibrium stimulus is denoted k , then the stimulus for adaptation is given by $f(\epsilon_{ij}) - k$, where ϵ_{ij} is the actual strain tensor. In general therefore, a mathematical law to describe adaptive bone-remodeling express the rate of change in mass as

$$\frac{dM}{dt} = C \{f(\epsilon_{ij}) - k\} \quad (1)$$

For strain-adaptive remodeling $f(\epsilon_{ij})$ is a nonlinear function and k is either (i) a function of the homeostatic strain (site-specific formulation) or (ii) an empirical material constant (site-independent formulation). For damage-adaptive remodeling, $f(\epsilon_{ij})$ is an integral function because microdamage is accumulative, and k represents the rate of damage repair.

The motive of damage-adaptive remodeling is to prevent unphysiological damage accumulation in the tissue, whereas strain-adaptive remodeling is a process that occurs to maintain an appropriate elastic energy transfer to the bone. Although both processes have a different motive, it is possible that the objective could be achieved using the same mechanism. Both approaches presume that there is a sensor in the bone which collects the mechanical stimulus and uses it to signal a biological response (Huiskes and Hollister, 1993). Several candidates have been proposed as sensors and it seems possible that the sensors are the osteocytes, contained in lacunae and connected to the bone surfaces via a dense canalicular network (Cowin et al., 1991).

In this study, the relationship between damage formation and local strain is explored to ascertain the extent that microdamage, occurring according to physiologically observed mechanisms, changes the local strain fields in the bone microstructure. If the changes are substantial enough, and if the osteocytes do indeed exist as strain sensors, then microdamage would stimulate bone remodeling using the osteocyte-sensor mechanism. If this were true, both elastic energy transfer (prefailure reversible processes) and microdamage accumulation (postfailure irreversible processes) would contribute simultaneously to the remodeling process (Fig. 1). To test this hypothetical relationship between microdamage and deformation behavior of osteocyte-containing lacunae, a finite element model of an osteon microstructure was generated, and used to analyze the consequences of various types of microdamage.

Methods

Model of the Osteonal Bone Microstructure. A finite element model of a cross-section of a whole osteon surrounded

by interstitial lamellar bone was generated using the MARC-MENTAT finite element code (Fig. 2). Generalized plane strain 4-noded finite elements were used, giving a total of more than 10,000 degrees-of-freedom. The geometrical attributes of the model were (i) osteon radius of 100 μm , (ii) Haversian canal radius of 20 μm , (iii) lamellae thickness of 5 μm , (iv) thickness of the "cement-line" between osteon and interstitial lamellae of 1 μm . There were therefore 16 lamellae per osteon. Dimensions of lacunae were taken from the work of Marotti et al. (1990). According to their measurements, osteocyte lacunae in lamellar bone could be represented by an ellipsoid whose principal axes have dimensions of $x = 9 \mu\text{m}$, $y = 22 \mu\text{m}$ and $z = 4 \mu\text{m}$ where the minor axis (z) is perpendicular to, and the major axis (y) forms an angle of 26-27 degrees with the longitudinal axis of the Haversian canal. Therefore, a cross section of an osteon will cut obliquely through an osteocyte lacuna. The planar dimensions of such a section through a lacuna is determined as an ellipse of major and minor axes equal to approximately 10 μm and 4 μm , respectively. Lacunae are located on the interface between two lamellae. Photographs of osteon cross-sections show that lacunae are evenly distributed, though no ordering pattern is apparent (e.g., Portigliatti Barbos et al., 1983). Lacunar density corresponding to the metaphyses of long bones of 2800 lacunae per mm^2 was used (Canè et al., 1982). Figure 2(a) shows a micrograph of an osteon cross-section and Fig. 2(b) shows the finite element mesh used in this study.

The orthotropic material properties of each lamellae were described as $E_1 = 17.26 \text{ GPa}$; $E_2 = 21.37 \text{ GPa}$; $E_3 = 29.76 \text{ GPa}$ where subscript 1 denotes the radial direction, subscript 2 denotes the angular direction and subscript 3 denotes the longitudinal direction (Katz et al., 1984). For the interstitial lamellae, subscripts 1 and 2 denote the thickness and plane of the lamellae, respectively. Cement-line mechanical properties are not known with certainty (Currey, 1984). However, it is thought to be less mineralized than the surrounding bone (Burr et al., 1988) and for this reason its Young's modulus is usually taken to be less than that of mineralized tissue (Hogan, 1992). A Young's modulus of 6 GPa and a Poisson's ratio of 0.25 was used.

Fig. 2(a) Microphotograph of an osteon cross-section (courtesy of Portigliatti Barbos et al. 1983)

Fig. 2(b) Finite element mesh of the osteon cross-section indicating the direction of the in-plane load. Boundary nodes are tied to displace equally in the direction normal to their surfaces. The lacunae chosen for sampling are indicated.

An axial load was simulated by applying a prescribed displacement to the z-direction degrees-of-freedom of the nodes of the generalized plane strain elements. A displacement to obtain a strain of $2000\mu\epsilon$ was applied since this strain level is representative of the stresses encountered in the mid-diaphysis of long bones such as the femur under several times body weight (Huiskes et al., 1981). A parametric analysis was carried out to determine the effect of the hoop stress applied in the in-plane y-direction to the upper face of the model, as shown in Fig. 2(b). A hoop stress of 10 MPa was used in this analysis as it is representative of hoop stress magnitudes at the mid-diaphysis level of long bones (Jacob and Huggler, 1980). The restraint condition was such as to keep the sides straight and orthogonal (by tying boundary nodes) to ensure that continuity is maintained between adjacent representative volumes.

Typical lacunae were sampled for analysis, located approximately perpendicular to the in-plane stress (Lacuna 1) and parallel to the in-plane stress (Lacuna 2), as indicated in Fig. 2(b).

Model of Damage Entities. Three damage mechanisms were analyzed in this study. The first is collagen bundle breakdown, which occurs when the collagen fibrils separate from the supporting hydroxyapatite crystals. This mechanism of damage was simulated using the continuum damage approach with a fractional reduction in Young's modulus as a damage variable (Lemaître, 1984). A series of analyses corresponding to a possible damage evolution sequence was carried, as shown in Fig. 3(a) and Table 1. The second damage mechanism investigated was interlamellar debonding. Four analyses corresponded to a sequence for interlamellar microcracking. The final loaded interlamellar microcrack configuration nearby a lacuna is shown in Fig. 3(b). The third damage mechanism investigated was microcracking in the cement-line. This was analyzed in five steps, ultimately leading to debonding of more than one quarter of the osteon circumference—the deformation of the final debonded configuration is shown in Fig. 3(c). Interlamellar debonding and cement-line debonding were simulated using gap elements, whereby nodes were uncoupled to allow frictionless sliding in response to a local shear stress and gap formation in response to a local tensile stress. To investigate the mechanical effects of loads and microdamage on osteocytes, the change of cross sectional area of the lacunae were calculated as a measure for osteocyte strain. The analyses were carried out for the undamaged microstructure, and for the microstructure subject to the various states of microdamage described above.

Results

The Haversian system and the lacunae have a stress concentrating effect in the bone tissue, as illustrated in Fig. 4. The formation of stress bands between lacunae is also evident—an effect predicted by Currey (1962). To quantify the fluctuation of stress and strain energy density in the bone microstructure, they are plotted as a function of the distance from the Haversian canal wall in Figs. 5(a) and 5(b), respectively. The extent which the microstructural features, such as the Haversian canal and the cement line, generate stress fluctuations can be seen. This effect would be greater in reality, since the present finite element model does not capture the complete microstructural irregularity of Haversian bone microstructure.

The cross-sectional areas of the lacunae were $267 \mu\text{m}^2$ before loading. After loading, the areas changed depending on locations. Their area values after application of the load increased by $6.19\text{E-}2 \mu\text{m}^2$ (Lacuna 1) and $4.46\text{E-}2 \mu\text{m}^2$ (Lacuna 2), respectively. The application of a hoop stress increases the change of lacunar cross-sectional area. This effect is illustrated in Fig. 6. In the absence of the hoop stress the change of lacunar cross-sectional area is smaller. Over the range of 0 to 10 MPa the cross-sectional area of Lacuna 1 changes by approximately a factor of two whereas that for Lacuna 2 changes by about 50

Fig. 3 (a) View of the region around a lacuna showing the zones and sequence of Young's modulus reductions used to analyse collagen bundle breakdown microdamage

Fig. 3(b) Final configuration of lamellar debonding around a lacuna. Lamellar debonding occurs progressively extending away from the lacunae.

Fig. 3(c) The final microcrack geometry and deformation for osteonal debonding microdamage [displacements $\times 50$]. Cement-line debonding begins at point A and progresses in both directions.

percent. However, even if the hoop stress is zero, lacunar cross-sectional area changes are significant.

Collagen-bundle breakdown (modeled as a reduction in Young's modulus in the finite element model) in the neighborhood of the lacunae changed the deformation of the lacunae under load. This effect is illustrated in Fig. 7. Such a result suggests that progressive microdamage accumulation in the la-

Table 1 Fractional reduction in Young's modulus for the simulation of damage evolution around lacunae (Fig. 3(b) shows the spatial distribution of damage evolution). Reduction of Young's modulus accompanies collagen-bundle breakdown type damage, and is used to analyze its mechanical effect.

	zone 1	zone 2	zone 3	zone 4
damage 1	0.25	0.125	0	0
damage 2	0.50	0.25	0.125	0
damage 3	0.75	0.50	0.25	0.125
damage 4	0.95	0.75	0.50	0.25
damage 5	0.95	0.95	0.95	0.95

mellae surrounding a lacuna can substantially change the behavior of the lacuna under load. For example, almost complete damage of the microstructure (95 percent damage extending approximately 20 μm along the lamellae either side of the lacunae) would cause a threefold increase in the cross-sectional deformation in the case of the lacuna oriented approximately perpendicular to the in-plane stress. Lacunae oriented approximately parallel to the in-plane stress are not so highly affected, with cross-sectional area increases of about 20 percent. Interlamellar debonding microdamage, which occurs as a gap opens along the interface between two lamellae, has a different effect on lacunar volume. This type of microdamage unloads the lacunae and reduces the deformation that it experiences towards zero, as illustrated in Fig. 8. Debonding of the cement-line unloads the osteon from the in-plane transverse deformations. The effect of this on lacunar deformation is shown in Fig. 9. Debonding adjacent to a lacuna increases lacunar deformation substantially whereas when the microcrack bypasses the lacuna its deformation reduces almost to zero.

Discussion

Before entering into a discussion of the results obtained above, we must first outline certain features of the modelling approach. First, the finite element model is only of the extracellular matrix and no attempt has been made to model the mechanism by which the cells themselves are stimulated. It is con-

Fig. 4 Stress distribution at a microstructural level in an osteon surrounded by interstitial bone. Only a quarter of the mesh is shown since the undamaged structure is symmetric. Sharp changes of stress occur at the cement sheath separating the osteon and the interstitial bone. The stress-concentrating effect of lacunae is also apparent.

RADIAL DISTANCE FROM THE HAVERSIAN CANAL

Fig. 5(a) Maximum and minimum principal stress as a function of distance from the Haversian canal wall.

RADIAL DISTANCE FROM THE HAVERSIAN CANAL

Fig. 5(b) Strain energy density as a function of the distance from the Haversian canal wall.

Fig. 6 The effect of the hoop stress on cross-sectional area change of lacunae loaded under 2000 μe compression. Two lacunae are sampled; lacuna 1 is oriented parallel to the in-plane stress and lacuna 2 is oriented perpendicular to the in-plane stress (location of lacunae is shown in Fig. 2(b).)

Fig. 7 The change in cross-sectional area of lacuna as the collagen bundles of the surrounding lamellae undergo a damage process under tension. The first set on the bar-graph represents the change in lacunar volume under load in the undamaged microstructure and the subsequent bar-sets represent increasing amounts of microdamage. (Location of lacunae is shown in Fig. 2(b).)

tured that the stimulus may originate due to fluid flow around osteocyte cells. Second, the structural model takes a planar section through what is a three dimensional structure. This only allows the in-plane deformations to be calculated and therefore the actual volume change of the lacunae cannot be calculated directly from the model. Third, we have not simulated the actual process of damage formation in the bone tissue. Rather we have presented an analysis of the consequences of damage were it to occur. Therefore the model is not meant to answer the question "Does damage occur?". Table 2 presents the interpretations of certain experimental studies of this question. Besides extensive *in vitro* studies, microdamage has been observed *in vivo*, although there are difficulties in separating actual microdamage that has arisen *in vivo* from artifacts introduced in specimen preparation (Burr and Stafford, 1990). The mechanisms described in Table 2 are those modeled in this investigation. Despite the above limitations, the model does give a picture of the local changes in the strain field caused by microdamage in Haversian bone for the first time. The results allow a more quantitative approach toward understanding the relationship between damage mechanisms, local strain changes and bone remodeling signals.

The stress distribution predicted in the osteon cross section is similar to that reported by Hogan (1992) in a study of Haversian bone as a composite material. In particular, sharp

Fig. 8 Effect of lamellar debonding on the cross sectional area of lacunae. (Location of lacunae is shown in Fig. 2(b).)

Fig. 9 Effect of cement-line debonding on the cross sectional area of lacunae. (Location of lacunae is shown in Fig. 2(b).)

stress changes at the cement-line are predicted as shown in Fig. 4 and Fig. 5(a). Figure 5(b) shows that the strain energy density is higher in the interstitial lamellae than in the osteon matrix because perhaps the more compliant cement-line shields the osteonal lamellae from the in-plane stress. This may be part of the reason why interstitial lamellar microcracking is more often observed *in vivo* than osteonal microcracking (Frost, 1960; Burr and Stafford, 1990; Schaffler et al., 1994). The formation of stress concentration bands of higher than average stress between lacunae is also predicted. This suggests that fracture propagation in cortical bone would follow a path between lacunae.

The osteocyte-sensory hypothesis proposes that the osteocytes contained in lacunae are stimulated as the lacunae deform in the local strain field. Central to this hypothesis is the assumption that the matrix deforms elastically, and therefore that the lacunae return to an equilibrium volume when the load is released. Cowin et al. (1991) suggest that, even though the strains generated in the mineralized matrix are very small, they would be sufficient to cause a fluid flow to stimulate the osteocytes. The predictions of the present model are that lacunae cross-sectional area does indeed change very slightly. Breakdown of the surrounding mineralized matrix will increase the area in the lacunae, substantially in some cases, as shown in Fig. 7. We can note that this type of damage is difficult to detect *in vivo* but it has been observed *in vitro* (Ascenzi and Bonucci, 1976). It must surely precede the for-

Table 2 Damage mechanisms observed after an *in vivo* cyclic dynamic load application and *in vitro* fatigue. Entries marked with an * denote those investigations in which the fatigue loading was applied *in vitro*.

INVESTIGATION	LOADING	OBSERVATION
Frost (1960)	cadaveric bone	"50% of the acceptable cracks examined occurred in the plane of the cement line"
Chamay & Tschantz, (1972)	<i>In vivo</i> dynamic overloading	* "... fibre bundles, normally aligned and adherent, are wrinkled and separated from each other"
Ascenzi and Bonucci, (1976)*	tension of single osteons	*"microfractures [of lamellae] are so tiny they can be visualised only by using the electron microscope"
Carter and Hayes, (1977)*	<i>In vitro</i> fatigue loading	* "... separation (or debonding) at cement lines and interlamellar cement bands. Occasional microcracking of interstitial bone ... fibrous bridging through cement bands"
Benelise et al. (1989) Cameron and Fornasier (1975)	cadaveric bone	Treabular fatigue fractures
Burr and Stafford, (1990)	cadaveric bone	"Microcracks ... unlike other discontinuities in bone being larger than canaliculi and smaller than vascular canals".
Stover et al. (1993)	<i>In vivo</i> dynamic overloading	"Microcracks were located parallel to and overlapped radially oriented collagen fibres"
Schaffler et al. (1994)	cadaveric bone	"Microcracks ... were in the interstitial bone or ran from interstitial bone into osteon cement lines (87%); ... microcracks completely within cement lines (11%)"

mation of macroscopic cracks which have been observed in vivo (see Table 2). It is known that microcracks in many man-made composite materials spend nearly all their lives as very short cracks (Hull, 1981). If this holds true for bone tissue, then the type of microdamage analysed here by reduction in modulus could be very common.

The predictions shown in Figs. 7–9 suggest that lacunae oriented parallel to the circumferential load are more affected by microdamage than those oriented parallel to the load. If the in-plane load is reduced to zero, the lacunae still deform in the plane due to the Poisson effect (Fig. 5). This suggests that the presence of significant circumferential loads, as occurs in the diaphyseal sections of long bones after hip replacement, for example, (Jacob and Huggler, 1980), could be an important factor in a adaptive-remodeling if remodeling is mediated by osteocytes.

It should also be mentioned that mechanisms for damage stimulated remodeling have already been proposed. Frost (1973) offers the idea that microdamage may trigger a remodeling response via the canalicular network surrounding the osteocytes. Martin and Burr (1989) hypothesize that microcracks trapped by Haversian systems may unload the surface of the Haversian canal wall triggering a response in the bone lining cells which cover that surface. This hypothesis is sustained by Prendergast and Huiskes (1994) who predicted substantial stress changes on the canal wall during cement-line debonding.

The osteocyte-sensory hypothesis has been used as a physiological basis for a mathematical model to simulate trabecular bone adaptation by Mullender et al. (1994). The remodeling signal is calculated as a function of the strain in the neighborhood of an osteocyte-containing lacuna. In this way the units of bone, responding independently, form a trabecular structure because each competes with its neighbor (Weinans et al., 1992). Because the results presented here show a significant relationship between lacuna deformation and local microdamage, we suggest that localized failure of bone "units" could be monitored by the same mechanism as is used to sense strain, and this effect could play a role in bone architecture formation and adaptation. Taking the example of trabecular fractures, this would mean that microdamage could stimulate an increased bone-remodeling rate if such an increase was necessary to prevent fracture of the trabecula. The picture emerges, not of two mutually exclusive mechanisms of damage-adaptive remodeling and strain-adaptive remodeling, but rather of complementary processes ensuring survival for units of bone tissue.

It is interesting to note that one effect of microcracking is to unload the lacuna local to the damage site (see Fig. 8 and Fig. 9). According to the strain-adaptive remodeling paradigm, this would lead to resorption. This leads to the following paradox: high loads lead to damage accumulation which causes local stress reductions and thus resorption. Therefore, high loading rates stimulate resorption. This conclusion fortunately concurs with the results of Burr et al. (1985) and Mori and Burr (1993) who correlated the presence of microcracks with resorption sites. The present results therefore give theoretical support to the experimental results of Mori and Burr (1993)—and further suggest that microcrack-stimulated resorption could be a local manifestation of strain-adaptive remodeling.

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