Bone, 10, 207–214 (1989)
Printed in the USA.

8756-3282/89 $3.00 + .00

Mechanical and Morphological Effects of Strain Rate on Fatigue of Compact Bone

M. B. SCHAFFLER,[1,2] E. L. RADIN[1] and D. B. BURR[1,2]

[1]*Departments of Anatomy and* [2]*Orthopedic Surgery, West Virginia University Health Sciences Center, Morgantown, WV*

Address for correspondence and reprints: Dr. Mitchell B. Schaffler, Division of Anatomy, M-004, University of California, San Diego, School of Medicine, La Jolla, CA 92093.

Abstract

Compact bone specimens were cyclically loaded in uniaxial tension for one million cycles; loading was performed at either of two physiological strain rates (0.01 s^{-1} or 0.03 s^{-1}) and a physiological strain range (0–1200 microstrain). Microdamage in loaded and nonloaded control specimens was then assessed histomorphometrically. Fatigue, evidence by stiffness loss, was observed at both strain rates and was significantly greater in specimens loaded at the high experimental strain rate than in specimens loaded at the low strain rate. Morphologically, this fatigue corresponded to increased numbers of microcracks in the bone. These data show that fatigue and resultant microdamage are realistic expectations of cyclic loading within the physiological strain range. The rate at which strains are developed influences the fatigue behavior of compact bone, suggesting that cyclic loading at high physiological strain rates, characteristic of vigorous activities, is more damaging to compact bone than loading at lower physiological strain rates.

Key Words: Compact bone–Fatigue–Strain–Strain rate–Microdamage.

Introduction

Fatigue in compact bone is the process of gradual mechanical failure caused by repetitive loading at stresses or strains far lower than those required to fracture bone in a single application of force. Fatigue processes are implicated in both the normal and pathological physiologies of the skeleton. In the former context, it is suggested that microdamage caused by fatigue of bone under normal loading is a principal stimulus to osteonal remodeling; the turnover process in cortical bone then serves to remove and replace bone which has approached the limit of its fatigue life (Frost 1966; Carter et al. 1981a,b; Martin and Burr 1982; Burr et al. 1985). Inadequacy of this fatigue repair response may lead to fractures. They may occur because damage is too extensive to be repaired by normal remodeling, as is thought to happen with "fatigue fractures" (Morris and Blickenstaff 1957; Devas 1975), because depressed remodeling processes cannot adequately repair normally occurring microdamage, as is postulated for osteoporotic fractures (Frost 1986), or because of some combination of these factors.

All these scenarios are predicated on the occurrence of fatigue processes as a consequence of normal physiological loading. Previous in vitro studies examined principally the effects of different stress or strain magnitudes on compact bone fatigue, at stresses or strains higher than those encountered with normal physiological loading (King and Evans 1967; Swanson et al. 1971; Gray and Korbacher 1974; Carter et al. 1976, 1981a, 1981b; Lafferty and Raju 1979; Carter and Caler 1983, 1985). These studies showed that compact bone fatigue is characterized mechanically by a progressive loss of stiffness and strength, leading ultimately to fatigue failure of the bone. Extrapolations from the studies of Carter et al. (1981a) and Carter and Caler (1985) suggest that loading at physiological stresses or strains should result in fatigue failure of compact bone after 10 million or more loading cycles. However, the actual fatigue properties of compact bone loaded at physiological stresses or strains are undetermined.

It is unclear how other aspects of the strain regime affect the fatigue behavior of compact bone. One parameter which is of particular interest is strain rate, as it varies considerably during physiological loading. Vigorous activities such as rapid walking or running are characterized by higher strain rates, as well as by higher strain magnitudes (Rubin and Lanyon 1982). Bone is viscoelastic, that is, there is a strain rate dependency for its mechanical properties (Carter and Hayes 1977a). Loading at higher strain rates will cause a relative increase in bone stiffness (Wright and Hayes 1976; Currey 1988; Schaffler and Burr 1988); increased stiffness is correlated with increased fatigue resistance in compact bone (Carter et al. 1981b). Conversely, loading at higher strain rates imparts more energy to the bone. This has been correlated with decreased resistance to fracture (Margel-Robertson and Smith 1978), and may reduce fatigue resistance as well.

Carter and Hayes (1977b) showed that the fatigue behavior of compact bone is like that in composite materials. It is characterized mechanically by a progressive loss of stiffness and strength (Salkind 1972; Hahn and Kim 1976; Agarwal and Broutman 1980; Reifsnider et al. 1983). Fatigue in composite materials is characterized microstructurally by widely distributed microdamage, including matrix microcracking, delamination, debonding and fiber pull-out, and void formation (Hahn and Kim 1976; Agarwal

and Broutman 1980; Reifsnider et al. 1983). Microcracking of bone matrix, separation of lamellae from one another (delamination) and separation of osteons from the surrounding bone matrix (debonding) all occur in cortical bone specimens which have undergone fatigue loading in vitro at strains and strain rates greater than those within the habitual physiologic range (Carter and Hayes 1977a), as defined by the in vivo strain experiments of Lanyon and colleagues (Lanyon et al. 1982; O'Connor et al. 1982; Rubin and Lanyon 1982; Rubin 1984). Frost (1960), Tschantz and Rutischauser (1967) and Burr et al. (1985) report microdamage in human post-mortem bone samples and samples from experimentally loaded animal skeletons. However, the actual relationship of this microdamage to more normal physiological loading of the skeleton is unclear.

Our objectives in the current studies were to examine the manner in which fatigue occurs in compact bone with cyclic loading in the physiological strain range and to determine the effect of different physiological strain rates on those fatigue properties. In the current studies we examined the early mechanical and morphological manifestations of compact bone fatigue behavior. We then sought to evaluate and quantitate microdamage resulting from fatigue processes that occur with cyclic loading in the physiological strain range.

Materials and Methods

Mechanical testing

Cortical bone test specimens were prepared from the mid-diaphyses of fresh femora and tibiae from 2–3 year old steers. Diaphyses were sawed into longitudinally oriented slabs using a bandsaw and these were turned on a lathe. Completed specimens had a 12 mm long uniform diameter (3 mm) gage length and tangentially blending filets to the grip ends (5 mm diameter). Specimen preparation, geometry and dimensions are summarized in Fig. 1. During all phases of preparation, specimens were under constant irrigation or immersed in physiological saline. Specimens were stored frozen at −20°C until testing; details of specimen geometry, fabrication and storage are consistent with procedures published elsewhere (Sedlin and Hirsch 1965; Wall et al. 1970) and are discussed in detail by Schaffler (1985). Ground cross-sections (100 μm thickness) were prepared from excess bone trimmed from the specimen ends and from these sections osteonal area fraction was measured by point counting. Whether specimens were comprised of primary (plexiform) or secondary osteonal bone was determined and the data ensured that all test groups were quantitatively equivalent with regard to microstructural types represented.

Prior to testing, specimens were thawed in physiological saline. Specimens were mounted in grip fixtures, which have a reservoir of low-melting point alloy to allow axial alignment of the specimens. Throughout the entire test, specimens were wrapped in saline-soaked gauze and continually wetted from a reservoir of normal saline. Specimens were tested at room temperature (21 ± 2°C) because of the constraints of the experimental apparatus; this may have systematically increased the fatigue resistance of the test specimens relative to testing at body temperature (Carter and Hayes 1976). Specimens were tested using cyclic loading in tension on an MTS closed-loop servohydraulic system (model 440, Materials Test Systems, Inc., Minneapolis, MN) with a built-in digital function generator. An axial extensometer (MTS model 232.26B) was attached to the gage length area of each test specimen in order to monitor its strain and loads were measured using the system load cell.

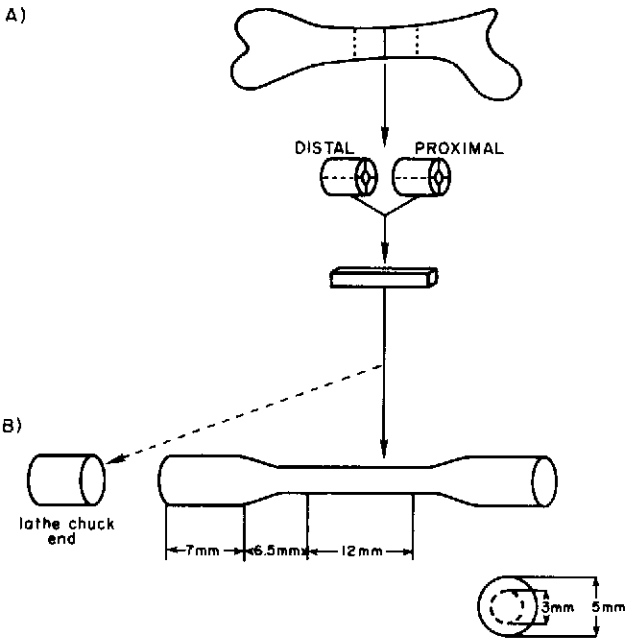

Fig. 1. Schematic summary of (A) the steps in preparation of compact bone test specimens from bovine long bones, and (B) geometry of final specimens.

Cyclic loading of bone specimens was performed in uniaxial tension under strain control. This allowed specimens to be tested with strain ranges and rates consistent with those measured directly by the application of strain gages in living animals. Specimens were loaded cyclically using a strain range of 0–0.12% (0–1200 microstrain); this approximates the peak range measured on tensile surfaces of long bones up to and during peak locomotory activities (O'Connor 1981; Rubin and Lanyon 1982; W. Caler unpublished data). Two strain rates were used to evaluate the effects of strain rate on compact bone fatigue: 0.01 s^{-1} and 0.03 s^{-1}, approximating those measured using in vivo strain gages during rapid walking and running, respectively, in dogs, horses and sheep (O'Connor 1981; Rubin and Lanyon 1982; W. Caler unpublished data). A triangular ramp wave was used for all loading (Fig. 2); a triangular ramp wave loading program was chosen because it allows both strain rate groups to be tested at the same strain range and loading frequency (4 Hz), by varying the off time and keeping the peak-to-peak period constant.

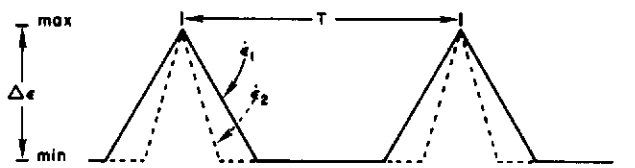

Fig. 2. Triangular loading regimes used in experimental loading of test specimens at low and high physiological strain rates ($\dot{\epsilon}_1$ & $\dot{\epsilon}^2$, respectively) at a single strain range ($\Delta\epsilon$). The off interval was varied, while peak-to-peak period (T) and therefore loading frequency was held constant for both strain rates.

Ten compact specimens were tested at each strain rate. Based on extrapolations from previous studies (Carter and Caler 1985), it was not expected that specimens would fall within less than 10 million loading cycles at the physiological strain range employed in the current experiments. Because complete failure was not anticipated, a defined stiffness loss criterion was used to evaluate differences related to loading for each experimental condition (Agarwal and Broutman 1980; Reifsnider et al. 1983). Fatigue was assessed by calculating stiffness loss over the one million cycle experimental loading period. During all loading, strain and load versus time were recorded continuously on an X-Y-Y chart recorder. In addition, load and strain levels were monitored on a storage oscilloscope during selected intervals. The specimen stiffness was defined as the stress range measured for the first load cycle divided by the strain range; specimen stiffnesses also were measured at intervals throughout the loading and on the final load cycle.

A group of loading-control specimens ($n = 6$) was examined to assess whether any change in the mechanical properties of test specimens occurred as a result of temperature or ambient condition effects during the time period required to load specimens for one million cycles (approximately 3 d). These specimens were mounted on the testing system and loaded to 1200 microstrain at 0.03 s^{-1} to determine initial stiffness; specimens were then left at zero strain for 3 d, at which time stiffness was measured again.

To determine whether significant fatigue, evidence by stiffness loss, occurred in control of either group of loaded test specimens, percentage decreases in specimen stiffness were tested against a null hypothesis of no decrease in stiffness (i.e., no fatigue). In order to provide the most conservative test, the null hypothesis of no decrease in stiffness was defined as 0.5% stiffness loss, rather than 0% stiffness loss, in order to account for measurement errors in the load and strain transducers. All comparisons were made using the Mann-Whitney U test (Siegel 1956); statistical significance is reported at the $p < 0.05$ level.

Histological evaluation

After mechanical testing was completed, the central gage areas of specimens were cut into 10 cross-sections of 1 mm thickness using a low-speed metallurgical saw; these thick sections were used to provide bulk material to minimize the damage introduced during section preparation. Tissue blocks were mounted on the ends of plexiglas cylinders using cyanoacrylate adhesive; these cylinders served as polishing and viewing mounts for light microscopic studies. Specimen surfaces were polished to a high luster finish, starting with 600 grit abrasive followed by progressively finer alumina slurries, with a final particle size of 0.05 μm (Schaffler 1985). To examine microdamage, specimens were imaged using a reflected light microscope equipped for differential interference contrast (DIC) microscopy, using a 16× magnification objective.

Some microdamage may have already been present in the bones from which the test specimens were derived. In addition, preparation of the specimens for mechanical testing and subsequent histology involves cutting and polishing steps through which microdamage could be introduced through mechanisms other than experimental loading. In order to control for artifactual and inherent damage, a group of nonloaded specimens ($n = 9$) was examined as morphological controls; these were prepared and handled in identical fashion to all other specimens, but did not undergo any loading.

For each specimen, all cross-sections were analyzed for microdamage. Microcracks were imaged through a video camera attached to the microscope and their video images (Fig. 3) were then traced directly onto a digitizing tablet interfaced to an IBM-XT microcomputer. The total viewing magnification was 796×. No data were collected within one field width (0.4 mm) of the edge of the cross-section. A computer-based image analysis system (Bioquant, R&M Biometrics, Nashville, TN) was used to determine: length (mm) of microcracks, surface density (S_a, mm crack length/mm sq bone area) and numerical density (N_a, number/mm sq) of microcracks (Weibel 1979). Microcracks had to possess well defined "characteristic crack-edges" to distinguish them from polishing defects (Fig. 3). Small crack-like structures, of which several in a given field had the same orientation, were considered to be cutting artifact and were not included in the data collection. No crack extending to the edge of a cross-section was counted, as these could represent surface defects introduced during the machining process and enlarged during specimen loading. Differences between cyclically loaded versus morphological-control groups were analyzed using the Mann-Whitney U test and significance is reported at the $p < 0.05$ level.

Results

Mechanical testing

Initial stiffness and percent decreases in stiffness for all specimen are summarized in **Table I**. Among those specimens in which fatigue was evident, the stiffness loss occurred gradually over the experimental loading period. No specimen progressed to fatigue failure within the one million cycle duration of the experiment. Stiffness losses were observed in both experimental groups; mean percent decreases in stiffness were 5.4 ± 1.7 (s.e.) versus 1.8 ± 0.8 (s.e.) when loaded at strain rates of 0.03 s^{-1} and 0.01 s^{-1}, respectively. The difference between the groups was statistically significant. When tested against a null hypothesis of no change in stiffness (i.e., no fatigue), stiffness loss was significant only in the high strain rate test group. Stiffness changes over time for the loading-control specimens averaged 0.07% (±0.3% s.e.) and did not differ from the transducer accuracy ranges (0.5%), which were verified at intervals throughout these investigations.

Microstructural changes related to loading

Examination of the experimental specimens after one million cycles of loading showed that several types of microdamage were evident. In primary bone specimens, damage was manifested principally as cracks in the nonlamellar portion of the plexiform bone and as separations (delaminations) of lamellar from nonlameller regions or adjacent lamellae (**Fig. 4**). In osteonal specimens, damage was observed as gap-like separations at osteon cement lines and as cracks propagating through the extraosteonal (lamellar and nonlamellar) bone into osteon cement lines (Figs. 3 & 4). In both primary and secondary bone specimens, cracks rarely were noted running across (obliquely or transversely to) lamellae; such cracks were considered to be cutting or polishing artifacts, as they either extended to the specimen

Fig. 3. Photograph of video monitor screen showing field of osteonal bone with superimposed video image analysis overlay. Arrow in the field indicates a microcrack running between the osteonal cement line and the extraosteonal (interstitial) bone. Original magnification from the specimen to the monitor screen = 796×.

surface or were one of several defects present with similar orientations. No quantitative attempt was made to separate microcracks into different categories based on type and microstructural association.

Experimental and control group means and standard errors for microdamage measurements are summarized in Fig. 5. Loaded specimens had greater numbers of microcracks ($\bar{X}$ = 4.04 ± 0.74 microcracks/mm^2 and 4.50 ± 0.57 microcracks/mm^2, at low and high strain rates, respectively) than in the nonloaded cntrol specimens ($\bar{X}$ = 2.99 ± 0.30 microcracks/mm^2); the difference between the high strain rate versus control groups was significant. Mean microcrack length did not differ among the low strain rate ($\bar{X}$ 0.079 ± 0.013 mm), high strain rate (0.080 ± 0.014 mm) or control (0.080 ± 0.013 mm) specimens. Surface densities of microcracks in the low strain rate group ($\bar{X}$ = 0.31 ± 0.06 mm/mm^2) and high strain rate group ($\bar{X}$ = 0.36 ± 0.06 mm/mm^2) were increased over control values (0.25 ± 0.04 mm/mm^2), consistent with the observation that total numbers of microcracks and therefore total length of microcrack surfaces were increased in loaded specimens. These differences were not statistically significant.

Discussion

Bones in vivo are subjected to dynamic and repetitive loads, characteristically at stresses and strains lower than those required to fracture bone by a single application of force; repetitive loading can lead to failure of a material through a progressive process called fatigue. In addition, these loads are incurred at varying rates, maintained for varying periods of time, vary in frequency and may be repeated several thousand times per day. Previous in vitro investigations have examined the nature of compact bone fatigue at different stress or strain levels (King and Evans 1967; Swanson et al. 1971; Gray and Korbacher 1974; Carter and Hayes 1977b; Carter et al. 1976, 1981a, 1981b; Lafferty and Raju 1979; Carter and Caler 1983, 1985), though at higher levels than encountered with normal physiological loading; fatigue has also been examined in context to the different microstructures of compact bone, that is, unremodeled primary bone versus seconary osteonal bone (Carter et al. 1976). The manner in which bone fatigues with loading in the physiological strain range, and the role of other aspects of the normal loading regime in fatigue processes is unclear.

In the current experiments, fatigue in compact bone occurred quite readily with loading in the physiological strain range, evidenced by a decrease in specimen stiffness. However, progression to failure was not observed in any specimen within the one million cycles of loading used in these experiments. The experimental strain range (0–1200 microstrain) at a strain rate of 0.03 s^{-1} is typical of the mechanical environment measured in vivo on tensile surfaces of long bones during running (O'Connor 1981; Rubin and Lanyon 1982; W. Caler personal communication). If one assumes a stride length of 3 feet for a running animal, each limb would be loaded every 6 feet. One million cycles of loading would correspond to running about 1150 miles. The current data suggest good resistance to fatigue failure for compact bone when loaded within the physiological strain range.

Carter et al. (1981a, 1981b) characterized the relationship between number of cycles to fatigue failure and strain or stress range. Using those empirically derived relationships, they found good agreement between their experimental fatigue life determinations and those previously

Table I. Specimen initial elastic moduli and percent changes in stiffness (%Δ) after one million cycles of loading.

	E(GPa)	% Δ	mean (s.e.)
0.01 s^{-1}			
1	19.9	0	—
2	26.2	0	—
3	24.0	−1.4	—
4	24.9	0	−1.8 (0.8)
5	24.5	0	—
6	26.0	−1.0	—
7	20.7	−2.6	—
8	18.1	−3.8	—
9	21.5	−7.9	—
10	14.9	−1.1	—
0.03 s^{-1}			
1	21.8	−2.4	—
2	22.1	−2.9	—
3	23.3	−3.5	—
4	22.8	0	−5.4 (1.7)*
5	25.2	−4.4	—
6	25.2	−14.5	—
7	15.7	−15.3	—
8	21.0	−7.0	—
9	19.1	0	—
10	18.1	−4.2	—
	E	%Δ after 3 d	
Control			
1	23.1	−0.3	—
2	19.9	0	—
3	24.3	−0.4	−0.07 (0.3)
4	22.8	+0.4	—
5	21.6	0	—
6	23.3	0	—

* Differs significantly from 0.5% change ($p < 0.05$).

done using human bone (King and Evans 1967; Swanson et al. 1971) and bovine bone (Gray and Korbacher 1974; Carter et al. 1976; Lafferty and Raju 1979), performed using a variety of different loading modes. Extrapolation from Carter et al.'s relationships to the strain ranges used in the current experiments (see equation 1, [Carter et al. 1981a]) predicts fatigue failure in about 12 million cycles. Similarly, Carter and Caler (1985) predict failure will occur in zero to tension fatigue loading between 10 and 100 million loading cycles for the same strain range as used in this study (1200 microstrain). The observation that failure does not occur after one million load cycles at peak physiological tensile strain range is consistent with expectations from previous studies. Significantly, the current data appear to be the first to confirm that the fatigue process is initiated with cyclic loading in the physiological strain range.

The current data indicate a strain rate dependency for fatigue. The role of strain rate in compact bone fatigue is of particular interest, as strain rate can vary over an order of magnitude during the normal locomotor loading repertoire of an animal (O'Connor 1981; Rubin and Lanyon 1982). Cyclic loading at the physiological higher strain rate examined here results in decreased fatigue resistance of compact bone. Several previous observations may explain these findings. Higher elastic modulus, as would result from loading a viscoelasic material like bone at higher strain rates (Carter and Hayes 1977a), means that specimens will be subjected to higher cyclic stress levels; increased elastic modulus and higher cyclic stresses have been correlated to reduced fatigue resistance in compact bone (Keller et al. 1985). Similarly, developing peak strain over a shorter period of time, as is the case with loading at a higher strain rate, requires that energy be absorbed more rapidly by the material being loaded (Burstein and Frankel 1968; Sammarco et al. 1971; Panjabi et al. 1973; Wright and Hayes 1976). This may cause more rapid fatigue or more severe damage to compact bone. Margel-Robertson and Smith (1978) indicate that this can be significant even over the small range of strain rates encountered with physiological loading; they show that the work-to-fracture of compact bone decreases markedly over a small range of strain rates. More recently, Currey (1988) demonstrated that strain rate actually has a much greater effect on the failure behavior than on the elastic properties of bone.

Strain rate also appears important to the control of bone remodeling processes. Experiments from our laboratory (Radin et al. 1986; Farkas et al. 1987) showed that with experimental loading of the hindlimb in rabbits at low strain rate, no alteration of bone was observed; at a strain rate equivalent to that examined here reactive remodeling and bone formation were initiated at the subchondral bone site studied. Similarly, O'Connor et al. (1982) demonstrated that osteonal remodeling in sheep long bone diaphyses is a function of strain rate as well. The current studies show that cyclic loading at high physiological strain rate is more damaging to bone than loading at a lower strain rate. The extent to which the bone remodeling observed in the above studies results from a direct biological effect of strain and strain rate on bone cell populations versus an indirect response to fatigue microdamage induced by cyclic loading at high strain rate warrants further investigation.

The test groups were composed of specimens of all types of bovine compact bone microstructures, that is, primary (unremodeled plexiform) bone and secondary osteonal bone, in order to provide a representative picture of how loading at physiological strains and different strain rates affects compact bone fatigue in general. Previous studies have shown that osteonal bone is weaker and less fatigue resistant than primary bone (Carter et al. 1976). Similarly, in the current studies, osteonal specimens at each strain rate generally showed greater stiffness loss than did primary bone specimens. Whether these differences would be significant at the strain range and rates examined here could not be assessed under the current experimental design, because of the small number of osteonal specimens used.

The nature of the fatigue process in cortical bone is essential to understanding the controls of the remodeling physiology of compact bone. Numerous investigators suggest that a principal function of osteonal remodeling is to resorb and replace a locus of bone which has approached the limit of its fatigue life, thereby restoring and maintaining structural integrity of the skeleton (Frost 1960, 1966; Tschantz and Rutischauser 1967; Chamay 1970; Swanson et al. 1971; Chamay and Tschantz 1972; Enlow 1976; Carter and Hayes 1981a, 1981b; Martin and Burr 1982; Burr et al. 1985). Carter and Hayes (1977b) showed that during cyclic loading of compact bone at high stresses, microcracking occurs within the structure. Fatigue microdamage is posited to be a signal for, if not a specific lesion directing, the initiation of a new remodeling unit in compact bone. Frost (1966) and later Carter et al. (1981a) suggested that microcracking damages osteocytes and their processes, thereby signaling the initiation of a new remod-

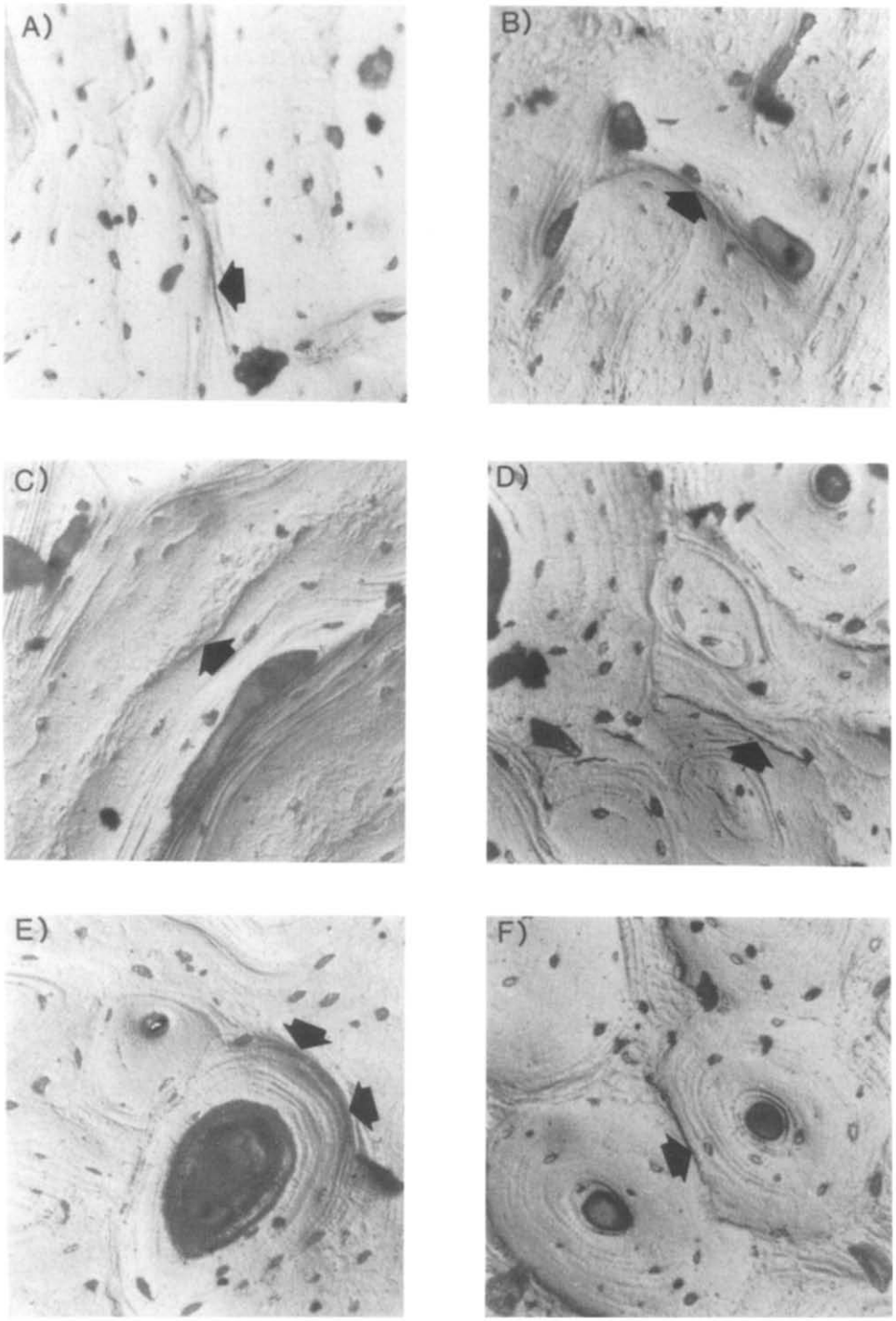

Fig. 4. Photomicrographs of various types of microdamage observed in compact bone test specimens; microdamage is indicated by arrows. In primary (plexiform) bone, microdamage was seen as separation type (delaminating) microcracks between lamellae (A) and lamellar-nonlamellar interfaces (B), and as cracks in the nonlamellar region of the bone (C). In secondary (osteonal) bone, microdamage was observed as cracks in the extraosteonal (interstitial) bone (D), as gap-type separations (debonding) of osteons from the surrounding bone matrix along the cement lines (E), and as cracks in the cement lines (F). Original magnification = 150×. (An example of a microcrack running from the interstitial bone to an osteon cement line is shown in Fig. 3.)

eling response, while Martin and Burr (1982) proposed that electrical potentials set up at microcrack edges signal osteonal remodeling to remove and replace the damaged region. These theories are predicated on the existence of fatigue, and its morphological correlate, microdamage, as a realistic expectation of the physiological loading environment. Frost (1960) cites microcracks in postmortem human bone biopsies as evidence that low-level fatigue processes occur in vivo. The actual nature and extent of microdamage resulting from cyclic loading in the physiological

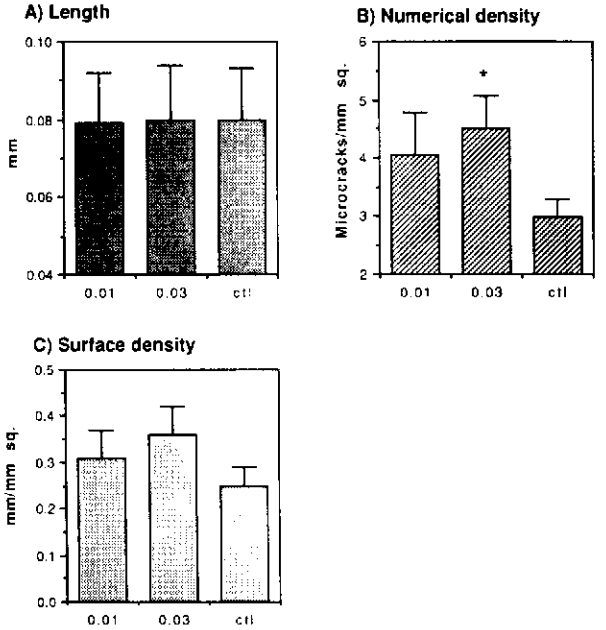

Fig. 5. Group means and standard deviations for (A) length, (B) numerical density and (C) surface density of microcracks in specimens loaded at the low experimental strain rate (0.01 s^{-1}), the high experimental strain rate (0.03 s^{-1}) and nonloaded control specimens (ctl). Asterisks indicate differences from the control group ($p < 0.05$).

strain or stress range is not known, nor has a cause and effect relationship between physiological loading and bone microdamage been established.

In the current investigation, microdamage was assessed in compact bone specimens using histomorphometric techniques. The principal observation is that loaded specimens had significantly greater numbers of microcracks than nonloaded controls. In addition, the relative numbers of cracks coincided well with the observed patterns of stiffness loss with cyclic loading. Specimens loaded at the higher experimental strain rate lost the most stiffness and had approximately 50% more microcracks than the nonloaded control specimens. Specimens loaded at the lower experimental strain rate lost comparatively less stiffness with cyclic loading; the number of microcracks in this group was increased only 35% over the control values.

Microdamage visible at the light microscopic level must have its origin at the ultrastructural and molecular levels. However, the nature of this ultrastructural and molecular damage is unknown. The direct relationship of ultrastructural and molecular microdamage to cortical bone remodeling remains a matter for conjecture. It may be that the increases in microcracking observed in the current loaded specimens represents, in part, an enlargement of "ultradamage" already present in the bone, but microcracks visible at the light microscopic level are currently of greatest interest, because of their proposed association with osteonal remodeling (Frost 1960, 1966; Carter et al. 1981a; Martin and Burr 1982; Burr et al. 1985).

The observation that the number of cracks increases with increasing "fatigue," while the length of microcracks remains unchanged, is consistent with the microstructural behavior observed with low stress (strain) cyclic loading dependent failure of other fiber-reinforced or laminated composite materials, such as fiber-reinforced graphite and laminated plastics (Agarwal and Broutman 1980; Reifsnider et al. 1983). In such materials, microdamage occurs early in the loading history, and the loss of material stiffness corresponds to increase in the number of cracks. These microcracks elongate only a finite amount because crack growth is limited by microstructural interfaces (layers or reinforcing fibers). Material stiffness then stabilizes. Very late in the loading history, microcracks can elongate past the inherent microstructural limits and failure can occur. By analogy, in the current experiments, early in the cyclic loading within the physiological strain range, microcracking in compact bone appears to be initiated at a number of loci. Elongation of microcracks would be limited by lamellar-nonlamellar bone interfaces in plexiform bone, by osteonal cement lines in secondary Haversian bone, and by lamellar interfaces in both bone types (Schaffler and Burr 1987; Burr et al. 1988). It is likely that studies of microdamage in bone specimens loaded close to their fatigue limit would show increases in microcrack length. However, within the early phase of fatigue examined here, the principal morphological manifestation of fatigue in compact bone appears to be increased numbers of microcracks, consistent with expectations based on the composite materials literature.

In conclusion, the current studies indicate that compact bone fatigue and resultant microdamage occur as a consequence of cyclic loading within the physiological strain range. The present study shows that the rate at which strains are developed influences the fatigue behavior of compact bone; cyclic loading at high physiological strain rate causes more damage than cyclic loading at a lower strain rate. Morphologically, these fatigue processes correspond to increased numbers of microcracks throughout the bone matrix. These data suggest that repetitive activities which are characterized by high strain rate, or more impulsive type loads like those characteristic of vigorous activities, may be more damaging to compact bone than activities which develop loading at lower physiological strain rate. That fatigue microdamage in compact bone can be caused by the relatively nominal cyclic strains characteristic of normal physiological loading provides support for the idea that some intrinsic repair mechanism, like osteonal remodeling, must exist in order to maintain structural integrity of the skeleton.

Acknowledgments: The authors thank Dr. L. E. Lanyon and W. E. Caler for supplying some of the in vivo strain gage data used in these experments. We also thank Vincent Kish III and Roger Miller for technical assistance. Portions of this work were presented at the 33rd Annual Meeting of the Orthopaedic Research Society. This work was supported in part by the West Virginia University Medical Research Fund, NIH Grants SO7-RRO-443-18 and AM 27127 and by the Orthopaedic Research and Education Foundation Grant 379-85.

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Received: September 2, 1988
Revised: February 2, 1989
Accepted: February 9, 1989