Time vs. Cycle Dependence of *Ex Vivo* Fatigue in Human Cortical Bone

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ABSTRACT

Although fatigue damage in bone has been recognized as a problem of clinical significance, few fracture mechanics studies have investigated how incipient cracks grow by fatigue in this material. In the present study, *ex vivo* cyclic fatigue experiments are performed in order to quantify fatigue-crack growth behavior in human cortical bone.

INTRODUCTION

Stress fractures of human cortical bone are a well recognized clinical problem with incidence rates of 1 to 4% reported [1-4]. As such fractures result from continued repetitive loading, rather than a single traumatic loading event, there have been many studies [5-21] on fatigue in cortical bone which have addressed issues of age, frequency, geometry, loading mode, damage accumulation, and *in vivo* remodeling and adaptation. Most studies have used a stress-life (*S/N*) approach where the life represents the cycles both to initiate and propagate a crack; as a result, results are difficult to interpret in terms of the responsible failure mechanisms as factors affecting initiation and growth cannot easily be differentiated. Consequently, here we adopt a fracture mechanics approach to specifically examine the propagation of pre-existing flaws in human cortical bone.

Surprisingly, there have only been two studies to date that have looked at fatigue damage in bone in this manner, specifically by Wright and Hayes [23] who measured crack-growth rates over a narrow range (~$7x10^{-7}$-10^{-4} m/cycle) in longitudinally-oriented specimens of bovine bone, and by Gibeling *et al.* [24], who reported growth rates between ~$6x10^{-10}$-10^{-5} m/cycle (with a Paris exponent of $m \sim 10$ [25]) in osteonal equine bone. No fatigue-crack growth rates have been measured for human bone.

Mechanistically, it is important to discern whether crack growth is a unique consequence of the repetitive cycling, or due to a succession of quasi-static fracture events driven by the maximum load, i.e., to discern whether damage is cycle- or time-dependent. Indeed, time-dependent crack growth under a sustained load has recently been reported for human cortical bone [26]. Attempts to address this question have been made by examining the role of frequency on *S/N* behavior; such analyses [5,12,27] suggest that tensile fatigue is may be time-dependent, since when data were plotted with respect to time, the effect of frequency on life was markedly reduced. To explain this, Carter and Caler [7], and Taylor [2] have suggested that there may be a transition in bone from a "creep"-dominated to a fatigue-dominated regime with decreasing stress levels.

Specifically, we characterize (for the first time) the *ex vivo* fatigue-crack growth behavior of human cortical bone, specifically in the proximal-distal direction, and seek to determine whether the fatigue damage is cycle- or time-dependent.

EXPERIMENTAL

Fresh frozen human cadaveric humeral cortical bone (donor age: 34-41 years, no known skeletal pathologies) was used, with blocks obtained by carefully sectioning the mid-diaphyses of the left humeri taken from each of the four donors. Fourteen compact-tension, C(T), specimens were machined from the humeri of four donors (Age(years)/sex: 34/female, 37/male, 37/male, 41/female); $N = 1$ was from the 34-year old female, $N = 11$ from the 37-year old males, and $N = 2$ from the 41-year old female, and were orientated with the nominal cracking direction along the proximal-distal direction of the humerus.

Samples were tested in Hanks' Balanced Salt Solution (HBSS) at 37°C, using sinusoidal 1 Hz loading at a load ratio of $R = 0.1$. Crack lengths, a, were monitored *in situ* using elastic unloading compliance, using solutions taken from [26]. A K-gradient of -0.08 mm^{-1} was used to operationally define fatigue thresholds, ΔK_{TH}, at 10^{-10} m/cycle.

To discern the role of static vs. cyclic fatigue mechanisms on subcritical crack growth, additional experiments were conducted involving a three-step, "fatigue/sustained load/fatigue" regimen, with all blocks performed at a fixed K_{max} value: (i) a block of *cyclic* fatigue loading at a constant ΔK value ($R = 0.1$, 1 Hz), (ii) a block of *sustained* loading at the same K_{max}, and (iii) a block of *cyclic* loading identical to the first block.

RESULTS

The variation in fatigue-crack growth rates with the maximum stress intensity, K_{max}, is shown for human cortical bone in Fig. 1, with data spanning more than five decades of growth rates. Regression analysis to a Paris power-law formulation [25] gave exponents of $m \sim 4.4$-9.5, well within the range reported for bovine and equine bone [23,24]. Fatigue thresholds, ΔK_{TH}, were in the range 0.45 to 0.6 MPa√m.

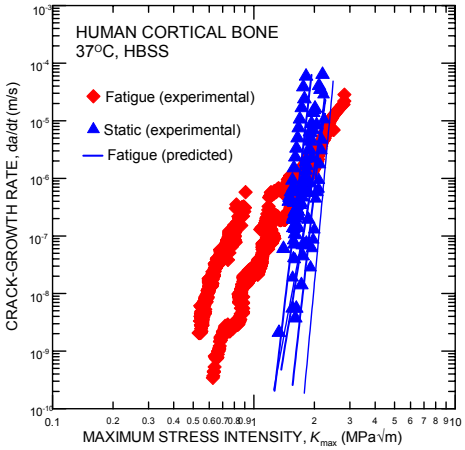

Fig. 1: Variation in *ex vivo* fatigue-crack growth rates, *da/dN* as a function of K_{max}, as compared to sustained-load cracking rates, for the proximal-distal orientation in human cortical bone.

Fractographic studies revealed the discontinuous nature of the crack path during fatigue, and specifically the presence of unbroken regions along the crack length, which act to bridge the crack and increase resistance to fracture by sustaining part of the load

that would otherwise contribute to crack advance. Such *uncracked-ligament bridges* can be as large hundreds of micrometers in size. The fatigue cracks did not penetrate the bulk of the osteon at any stage; indeed, the path taken by the crack was totally dictated by the cement line, i.e., the interface of the osteonal system with the surrounding matrix [26]. It was also apparent that cracks experienced a time-dependent crack-blunting phenomenon at the slower growth rates, consistent with observations in human cortical bone [26], and dentin [28,29]. Fracture surfaces appeared similar in both fatigue and overload failure.

Results from the "fatigue/sustained load/fatigue" tests, described above, were conducted at two specific (constant) K_{max} levels: (i) K_{max} = 1 MPa√m, corresponding to a (lower) growth rate where crack blunting was apparent, and (ii) K_{max} = 1.65 MPa√m, corresponding to a (higher) growth rate where no crack blunting was seen. Crack extension (Δa) *vs.* time (t) data are shown in Figs. 2a-b. At K_{max} = 1.65 MPa√m, crack growth was observed during all three loading blocks, with crack velocities (with respect to time) being relatively similar whether or not the loading was sustained or cyclic (Fig. 2b). In contrast, at K_{max} = 1 MPa√m, subcritical crack growth was undetectable during the sustained-load portion, but restarted once the fatigue cycling was resumed (Fig. 2a). This strongly implies that at the lower growth rates, it is not the maximum stress itself, but the process of fatigue cycling - repeated loading and unloading between the maximum and minimum stresses - that drives crack growth, i.e., subcritical cracking in bone in this low growth-rate regime is truly cycle-dependent. Conversely, at the higher growth rates, the magnitude of the maximum stress is high enough to drive crack growth almost in the absence of cycling; this implies that subcritical cracking in bone in this higher growth-rate regime is both cycle- and time-dependent. Such results strongly support the notion of a "transition" in the salient mechanisms responsible for subcritical crack growth in bone, from static-load (or "creep") dominated to cyclic-load (fatigue) dominated mechanism(s), with decreasing growth rates and stress-intensity level.

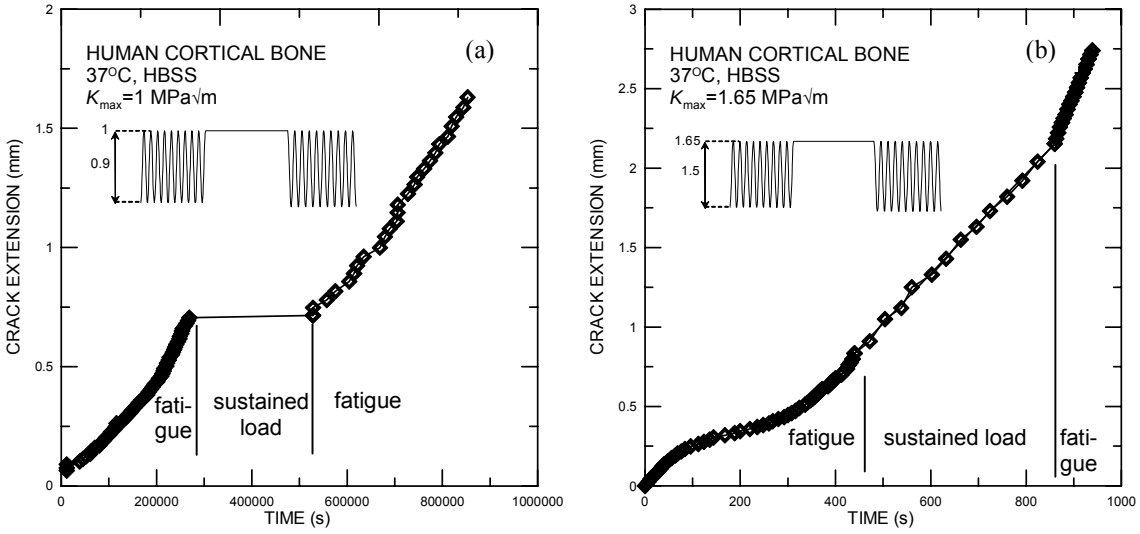

Fig. 2: Results of the "fatigue-sustained load-fatigue" tests at fixed K_{max} levels, presented as plots of crack extension as a function of time, for (a) K_{max} = 1 MPa√m, (b) K_{max} = 1.65 MPa√m.

Similar experiments where the frequency was changed at constant ΔK from 1 Hz to 10 Hz and back to 1 Hz at high (= 1.5 MPa√m) and low (= 0.9 MPa√m) ΔK levels, i.e., above and below the "transition" described above, showed that at the high ΔK levels. growth rates, expressed in terms of *da/dt*, were comparable at both frequencies, again consistent with a significant time-dependent contribution to crack growth. In contrast, at low ΔK levels, growth rates, expressed either as *da/dt* or *da/dN*, are higher at the lower frequency of loading, implying that the fatigue mechanisms involved in this regime have a more significant cycle-dependence and lessened time-dependence.

DISCUSSION

Several authors [2,6,12] have posed the question whether fatigue fracture in bone under cyclic loads is actually cycle- or time-dependent; their results, however, have invariably been inconclusive. The aim of the present work has been to address this issue by focusing solely on crack-growth behavior and discerning whether the *ex vivo* fatigue-crack propagation behavior measured in human cortical bone (Fig. 1) results from a true cyclic fatigue mechanism, or is simply caused by time-dependent, sustained-load cracking driven by the maximum load of the fatigue cycle.

We offer three approaches to help resolve this issue. The first of these is the constant K_{max} "fatigue-sustained load-fatigue" experiments shown in Fig. 2. The results of these experiments provide *an unambiguous demonstration of a true cyclic fatigue effect in human cortical bone at low growth rates*, specifically at K_{max} = 1 MPa√m. This is apparent by examining the Δa vs. t data at the end of the first (fatigue) block in Fig. 2a - holding the load constant at the fixed K_{max} level causes no crack extension; the crack will only continue to propagate if the loads are unloaded (and cycled). However, at higher growth rates, at K_{max} = 1.65 MPa√m (Fig. 2b), the crack propagates subcritically under both sustained and cyclic loading at nominally similar rates. This would imply that subcritical crack-growth rates in bone at higher stress intensities involves contributions from both time-dependent ("creep") and cycle-dependent (fatigue) mechanisms, with static mechanisms dominating.

The second approach involves experiments where the frequency was changed, from 1 to 10 and back to 1 Hz during cycling at constant ΔK. It is apparent from these experiments that the significant time-dependent contribution to cracking, seen at high ΔK by *da/dt* being approximately independent of frequency, is much reduced at low ΔK, where crack-growth rates (*da/dN*, *da/dt*) are lower at the higher frequency. Such experiments where the frequency is changed rarely can give conclusive evidence on the question of cycle- vs. time-dependence; however, our results clearly indicate that the time-dependent contribution to fatigue-crack growth is diminished in the low ΔK regime.

Finally, in order to more fully characterize the range of driving forces over which cyclic effects dominate, a third approach is utilized whereby the cyclic fatigue-crack growth rates are "predicted" solely from sustained-load cracking data (taken from [26]). The predictions are based on the methodology of Evans and Fuller [30] for materials that show *no true cyclic fatigue effects*, i.e., on the premise that there is no effect on crack extension specific to cyclic loading and that fatigue-crack growth is merely the sum of the increments of sustained-load (static) cracking associated with each fatigue cycle. If these "predicted" and the experimental growth rates correspond well, the inference is that

no true cyclic fatigue effect exists; however, if at a fixed ΔK the experimentally measured rates exceed the "predicted" rates, then this implies that cycle-dependent fatigue mechanisms are active.

Such "predictions" are shown as the lines in Fig. 1. At low crack-growth rates (~3 x 10^{-10} to 5 x 10^{-7} m/cycle), the measured fatigue-crack growth rates (at a given K_{max}) clearly exceed the predicted rates, whereas at higher growth rates (~5 x 10^{-7} to 1 x 10^{-5} m/cycle), the predicted rates are similar to slightly faster. This provides strong evidence that at low growth rates, a true cycle-dependent fatigue mechanism is operating in bone, whereas time-dependent sustained-load mechanisms appear to be more important at higher growth rates, the transition occurring between ~10^{-7} and 10^{-6} m/cycle. These observations are entirely consistent with results of the "fatigue-sustained load-fatigue" and "1 Hz/10 Hz/1 Hz" experiments described above. At low growth rates at a K_{max} of 1 MPa√m, conditions are clearly below the transition and cycle-dependent mechanisms control fatigue-crack growth; a K_{max} of 1.65 MPa√m is above the transition where sustained-load (static) mechanisms become active. This transition from static ("creep"-dominated) to cyclic (fatigue-dominated) mechanisms is similar to that suggested previously [2,7], although the present study provides the first conclusive evidence of the effect, and establishes the stress-intensity range where this transition occurs.

CONCLUSIONS

Based on an investigation of the *ex vivo* fatigue-crack growth behavior of hydrated human cortical bone in 37°C Hanks' Balanced Salt Solution in the proximal-distal direction, the following conclusions can be made:

1. The first fatigue-crack growth results for human cortical bone are presented for a cyclic frequency of 1 Hz and display a Paris power-law dependency, i.e., crack-growth rates are proportional to a power-law function of the stress intensity range, with an exponent of 4.4 to 9.5.
2. Observations of the crack paths showed crack propagation to occur preferentially along the cement lines of the secondary osteons. Uncracked-ligaments bridges were observed to form in the crack wake; in addition, crack tips were seen to become progressively blunter with decreasing crack-growth rates.
3. It was unambiguously determined that a "true" cycle-dependent mechanism is active for fatigue-crack growth in cortical bone under cyclic loading conditions. Although crack extension at high crack-growth rates involves a significant contribution from time-dependent mechanisms, there is a definitive transition to cycle-dependent mechanisms with decrease in growth rates. By comparing measured fatigue-crack growth rates with those "predicted" by integrating sustained-load (static) cracking data over the course of the fatigue loading cycle, the transition was found to occur at ~5 x 10^{-7} m/cycle.

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