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Short communication

Near-terminal creep damage does not substantially influence fatigue life under physiological loading

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ABSTRACT

Cortical bone specimens were damaged using repeated blocks of tensile creep loading until a near-terminal amount of creep damage was generated (corresponding to a reduction in elastic modulus of 15%). One group of cortical bone specimens was submitted to the near-terminal damage protocol and subsequently underwent fatigue loading in tension with a maximum strain of 2000 με (Damage Fatigue, $n=5$). A second group was submitted to cyclic fatigue loading but was not pre-damaged (Control Fatigue, $n=5$). All but one specimen (a damaged specimen) reached run-out (10 million cycles, 7.7 days). No significant differences in microscopic cracks or other tissue damage were observed between the two groups or between either group and additional, completely unloaded specimens. Our results suggest that damage in cortical bone allograft that is not obvious or associated with a stress riser may not substantially affect its fatigue life under physiologic loading.

1. Introduction

Massive cortical bone allografts are utilized in orthopedic surgery to reconstruct large defects in long bones. Allograft that fail tends to do so within 3 years following implantation (Mankin et al., 1996). The underlying mechanism that leads to early failure of allografts is not yet understood. Microscopic cracks and other damage may be present in otherwise normal donor tissue (Burr et al., 1997) or generated as a result of loads/stress concentrations generated during surgery (Akkus and Rimnac, 2001). The crack-limiting effects of bone ultrastructure prevent small cracks from propagating (O'Brien et al., 2005); however, it has been proposed that larger patches of microscopic damage (larger microcracks, larger regions of diffuse damage, etc.) are more likely to propagate under activities of daily living (Enneking and Campanacci, 2001; Sobelman et al., 2004; Wheeler and Enneking, 2005), suggesting that pre-existing microscopic tissue damage may influence early allograft failure.

Our long-term goal is to understand the mechanism behind the early fracture of large allografts. In this study we determine if severe loading applied to cortical bone impairs the fatigue life under subsequent loading at physiologic magnitudes.

2. Materials and methods

Bilateral femora from a 48 years old male donor (A) and a 49 years old male donor (B) were obtained from a donor bank (MTF). Specimens from the mid-diaphysis of the bones were prepared with a gage region of 15 mm × 3 mm × 1 mm (Joo et al., 2007). The specimens were randomized into testing groups, wrapped in saline soaked gauze, and stored at −20°C until testing.

Six specimens were used to identify a creep loading approach to generate near-terminal damage. A creep damage protocol adapted from Joo et al. (2007) was used (Fig. 1). The creep damage protocol consisted of: (1) an initial diagnostic cycle to measure elastic modulus (Young's modulus) consisting of a ramp to 0.1% tensile strain (at 0.1% strain/s) followed by immediate unloading; (2) a tensile load applied to the specimen at 40 N/s to a strain of 5000 με for 90 s after which the specimen was unloaded at 40 N/s and held at zero load for a period of 5 min to allow relaxation (85% of creep strain is relaxed over this time period) (Joo et al., 2007); and (3) a final diagnostic cycle to measure the Young's modulus following the creep damage cycle. Specimens underwent blocks of creep loading until failure and a near-terminal damage condition was identified based on reductions in Young's modulus.

Two groups of specimens were used to test the idea that near-terminal creep damage greatly reduces fatigue properties. The Damage Fatigue group ($n=7$) underwent blocks of creep loading to generate near-terminal damage as described above. The Control Fatigue group ($n=5$) was not pre-damaged prior to fatigue loading. Specimens from both groups were cyclically loaded in tension to a maximum load that corresponded to an initial strain of 2000 με (the high end of physiological strains) (Burr et al. 1996). Cyclic loading was applied at 15 Hz using a sine wave with a load ratio of $R=0.1$. Specimens were loaded until failure or run out (10 million cycles, 7.7 days).

Mechanical testing was performed on an Instron 8501 (Instron Norwood, MA) or a Bose Enduratec ELF 3400 (Bose, Eden Praire, MN) with a 100 lbs load cell. Strain was recorded during pre-damage using a mini-extensometer (Model 3442, Epsilon Tech., Jackson, WY). Mechanical testing was carried out at a temperature

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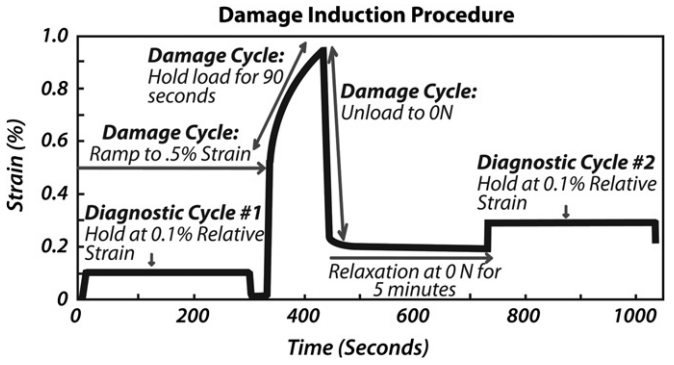

Fig. 1. A single block of the creep damage protocol is shown. Specimens in the Damage Fatigue group were submitted to repeated blocks of tensile creep loading to generate a near-terminal damage state.

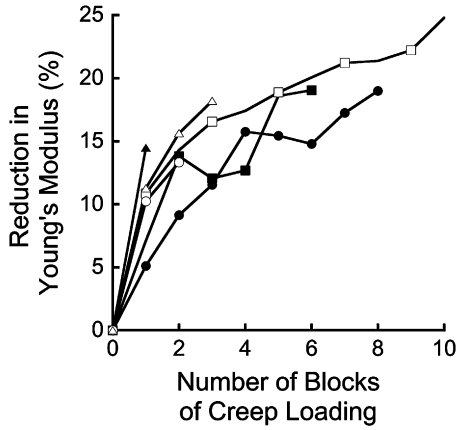

Fig. 2. Percent reduction in elastic modulus following a block of creep loading is shown (one block of creep loading is shown in Fig. 1). A 15% reduction in elastic modulus was selected as a near-terminal amount of damage since after exceeding this threshold additional blocks of creep loading are likely to result in specimen failure.

of 37°C using a saline drip containing protease inhibitors to reduce postmortem degradation (Bowman et al., 1998).

The gage length of each specimen was bulk stained for microscopic tissue damage using basic fuchsin (Burr and Hooser, 1995). Eight transverse sections were cut from the gage region, polished to 100 μm thickness and evaluated at 100× magnification to measure microscopic tissue damage. Microscopic tissue damage was quantified as diffuse damage (expressed as percent of diffuse damage area, DV/BV) and linear microcracks (expressed as cracks per unit bone area, Cr.Dn). Additional specimens ($n=10$) that were prepared in the same manner but not submitted to loading were evaluated for microscopic tissue damage (referred to as the unloaded control group). Comparisons among groups were made using ANOVA with $p<0.05$ classified as significant. Differences in rates of failure during fatigue loading were determined using a one-tailed Fisher's Exact test.

3. Results

Specimens failed after 1–12 blocks of creep loading (Fig. 2). The number of blocks of creep loading to failure was not related to specimen apparent density or donor. A 15% reduction in Young's modulus was selected as a near-terminal loading threshold because a subsequent block of creep loading would result in failure of 50% of the specimens.

Two specimens in the Damage Fatigue group failed while being submitted to the creep damage protocol and were removed from the study. Specimens that completed the creep damage protocol experienced 2–6 blocks of the creep damage loading resulting in a $15\pm1\%$ reduction in Young's modulus. One specimen in the Damage Fatigue group failed prior to the run out criteria

Table 1
Young's modulus and cycles to failure for each specimen are shown along with measures of microscopic tissue damage following loading. No significant differences in diffuse damage or crack density (Cr.Dn) were observed between groups.

Donor	E_0 (GPa)	E_d (GPa)	Reduction in E (%)	Diffuse damage DV/BV (%)	Cr.Dn (#/mm^2)
A	9.52	9.52	0.00	0.034	0.00
A	11.86	11.86	0.00	0.015	0.00
B	18.44	18.44	0.00	0.002	0.80
B	18.30	18.30	0.00	0.023	0.38
B	18.80	18.80	0.00	0.013	0.49
A[a]	11.00	9.33	15.18	0.035	0.00
A	10.53	9.05	14.06	0.043	0.00
A	9.35	8.00	14.44	0.033	0.00
B	14.90	12.60	15.44	0.045	0.96
B	21.00	17.90	14.76	0.006	1.72

A and B refer to donor. E_0=original Young's modulus. E_d=Young's modulus prior to fatigue testing (after any damage had been applied).

[a] Failed under fatigue loading, all other specimens reached the run-out condition.

(at 7,692,030 cycles). None of the specimens in the Control Fatigue group failed prior to the run out condition (Table 1). No differences in rate of change in peak-to-peak displacement during cyclic loading were observed between groups. Specimens in the Damage Fatigue group were not more likely to fail under fatigue loading ($p=0.50$). The amount of microscopic tissue damage in loaded specimens (Table 1) was not significantly different from that observed in unloaded controls (Cr.Dn$=0.122\pm0.177$, DV/BV$=0.029\pm0.020$, mean $\pm$ SD) (Fig. 3).

4. Discussion

We found no difference in fatigue life or microscopic tissue damage between the Damage Fatigue and Control Fatigue groups. The current sample size ($n=5$) was sufficient to detect a failure rate of 4 in 5. An increase in sample size to $n=20$/group (40 weeks of experimentation) would be required to detect a significant difference between the two groups assuming the same failure rate (1 in 5, $p=0.053$). Although the sample size is small, two aspects of the current study support the idea that the applied pre-damage does not *substantially* influence the clinical performance of allograft: first, the pre-damage is near-terminal in that additional loading is expected to lead to failure of 50% of all specimens. Only a portion of allografts would survive more pre-damage than was applied here and not be disqualified for clinical use as damaged. Second, the reduction in fatigue life caused by pre-damage, while not statistically significant, may be functionally significant since the number of cycles applied (10 million) corresponds to the number of load cycles in 3–10 years patient activity (Schmalzried et al., 1998) and allografts that do not fail within 3 years after implantation typically have a lifespan greater than 20 years (Mankin et al., 1996).

Although previous authors have run high cycle fatigue tests at physiologic strains in bovine bone (Schaffler et al., 1990), to our knowledge, our study is the first report of 10 million cycles of loading at physiological strains in human bone. Longer periods of testing may not be possible in the laboratory without postmortem degradation. We used a loading frequency roughly 10 times greater than physiologic loading (15 Hz). It has been observed that the fatigue life of cortical bone was not frequency sensitive, but rather depended on the duration of the test, under sinusoidal loading between 0.2 and 2 Hz (Caler and Carter, 1989). However, others have found little difference in fatigue life at higher frequency

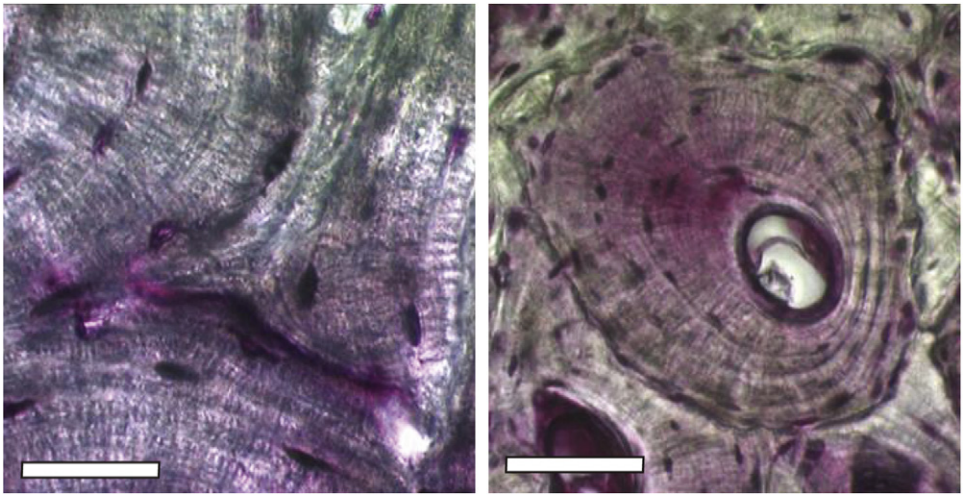

Fig. 3. Examples of (Left) a microcrack and (Right) diffuse damage in cortical bone are shown. The scale bars are 100 μm in length. No differences in the amount of stained microdamage were observed between the Damage Fatigue groups, the Control Fatigue group and completely unloaded controls.

(below 30 Hz) (Lafferty, 1978; Lafferty and Raju, 1979) supporting the use of high frequency loading to mimic years of activity.

We did not observe a significant difference in microscopic tissue damage between groups, a finding that is consistent with prior work, suggesting that there is a threshold of applied creep loading before microscopic damage becomes apparent (Jepsen et al., 1999). Our results suggest that the applied loading is not associated with increased microscopic tissue damage (measured by histology). Prior work has shown that fatigue loading at larger strain magnitudes generates greater amounts of microscopic tissue damage (Schaffler et al., 1989; Sobelman et al., 2004; Diab and Vashishth, 2005; George and Vashishth, 2005). Additionally, examination of whole bones under fatigue loading suggests that there may be a threshold of reduction in Young's modulus before the generation of observable increases in microscopic tissue damage (Burr et al., 1998). The precise relationship between reductions in Young's modulus and the amount of microscopic tissue damage remains unknown. With regard to the current study, it is important to note that detection of microscopic tissue damage may be limited due to the types of damage detectable by en bloc staining or differences and any differences in microscopic tissue damage type generated under tensile creep (as compared to the more commonly examined fatigue loading). Additionally the work did not include the effects of stress risers in the tissue (drill holes, etc.). Our results may have clinical implications, which suggest that cortical bone allograft that has undergone mechanical damage during the donor's lifetime that is not obvious on inspection may not substantially reduce allograft lifespan.

Conflict of interest statement

The following authors report no relevant conflicts of interest: Dr. Stern, Ms. Brinkman, Dr. Furmanski. Dr. Hernandez and Dr. Rimnac have received peer-reviewed research grant funding from the Musculoskeletal Transplant Foundation. Dr. Rimnac serves on the Board of the Orthopaedic Research Society.

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