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Distribution of microcrack lengths in bone *in vivo* and *in vitro*

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ABSTRACT

It is well known that bone contains small cracks; *in vivo* these microcracks are constantly growing and being repaired. Too rapid crack growth leads to stress fractures or fragility fractures. *In vitro*, changes occur in this population of microcracks when subjected to cyclic loading up to and including failure. Normally, the only parameters reported from such investigations are the number density of cracks and their average length. In the present work we examined the microcrack population in more detail. We analysed ten different sets of experimental data including *in vivo* and *in vitro* microcracks, plus two theoretical simulations. We showed for the first time that the distribution of crack lengths can be described using the two-parameter Weibull equation. The values of the two constants in the equation varied depending on bone type/species and showed consistent trends during *in vitro* testing. This is the most detailed study to be conducted on microcrack populations in bone; the results will be useful in future studies including the development of theoretical models and computer simulations of bone damage and failure.

1. Introduction

Stress fractures and fragility fractures in bone are a major cause for concern, especially in relatively active individuals and those whose bone strength is compromised. For example, military recruits suffer high rates of stress fractures during training (Bloomfield et al., 1995) and 5%–15% of all injuries to runners are caused by stress fractures (Guten, 1997). Fragility fractures occur predominantly in people suffering from osteoporosis: in the UK 200,000 such fractures occur each year and worldwide fracture rates are predicted to rise to 6 million within 50 years. Between 2.5% and 12% of people aged 65 or over will suffer a fracture by falling, and a third of women and one in 12 men over 50 years will suffer an osteoporosis-related fracture at some time in their life (Campbell et al., 1999).

Stress fractures occur as a result of fatigue mechanisms caused by the action of cyclic stress, which leads to the formation and growth of microcracks, especially when bone is loaded in compression, which is the predominant loading mode *in vivo* (Currey, 2002). Bone is a material in which cracks readily form, but find it difficult to grow, and they tend to remain small and follow the direction of easy growth, parallel to lamellae and osteons, which is approximately parallel to the longitudinal axis in the long bones (Martin and Burr, 1998). Microcracks were first observed by Frost (1958), (1960) who correctly hypothesised that one of the functions of bone remodelling is to repair the tissue by removing these cracks. Since then many workers have observed and measured microcracks; the great majority of these studies involved detecting cracks by microscopic examination of transverse sections cut from bones *ex vivo* or from test samples after *in vitro* cyclic loading. The parameters normally presented in publications are the number density, expressed as the number of cracks per unit area (rather than the true density which would be per unit volume) and the average crack length. Another parameter, the surface crack density, records the total crack length per unit area, this being simply the product of the other two parameters (Fazzalari, 1998; Frank, 2002; Muir et al., 1999; Norman and Wang, 1997).

Some workers have attempted to observe and record the rates of growth of individual cracks during cyclic loading (Akkus and Rimnac, 2001; Kruzic and Ritchie, 2008), though till date this kind of work has received little attention. There have also been some attempts to develop theoretical models and computer simulations of their growth (Taylor and Lee, 2003). The threshold for crack formation and the mechanisms responsible for initiating microcracks are still poorly understood (Bloomfield et al., 1995), and this is a major limitation in the development of theoretical models.

The normal description of bone damage in terms of the two parameters described above—crack density and average crack length—omits information about the distribution of crack lengths

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within the sample observed. We reasoned that this extra information might be useful in understanding the development of damage and eventual failure and in formulating theoretical models and simulations. We hypothesised that the distribution of crack lengths could be described by some standard form such as a Weibull or Gaussian distribution. If so, since this distribution can be fully described by a small number of constants, we hypothesised that the values of these parameters, which essentially characterise the state of damage in the material, would vary in a systematic way with parameters such as the type of bone, the type of animal and the loading conditions, whether *in vivo* or *in vitro*, such as the applied stress range and number of cycles. The aims of the present work were to investigate these hypotheses using data from our own experimental work and that of others.

2. Materials and methods

We collected data on the lengths of individual microcracks, using results obtained previously from our research group, consisting of *in vivo* ovine bone data (Khan, 2010), bovine bone data from work published previously (O' Brien et al., 2003) and bovine bone data obtained from new tests as described below. We also contacted other researchers, who had published work in this field (Burr, 1998; Gellasch and Kalscheur, 2002), who kindly agreed to provide us with their original crack length measurements which had not appeared in their publications. These studies recorded crack lengths either from bones which had been subjected only to *in vivo* loadings or else bones (or test specimens made from bones) which were subjected to additional cyclic loading *in vitro*, at some specified range of stress or strain for a specified number of cycles.

Table 1 summarises the test conditions in each case. The definition of microcrack length is the distance between the two tips of the crack as seen on transverse sections. The range of stress or strain is defined as the difference between the maximum and minimum values in the cycle imposed.

These data cover a useful range of loading conditions, from *in vivo* loading, which typically includes strains up to 2000–3000 με (Rubin and Lanyon, 1985), equivalent to a stress range of approximately 40–50 MPa, to *in vitro* testing at higher stress ranges up to 80 MPa. Results obtained by Burr and Milgrom (1996) reported slightly less than 2000 με when measuring tibial shafts of soldiers during intensive training regimes. The highest strains registered *in vivo* are the results obtained by Nunamaker et al. (1990), measuring compressive strains in racehorses ranging from 4400 to 5670 με. In addition one should remember that *in vivo*, microdamage is being continuously repaired, whilst *in vitro* this is not the case, so there could be differences in the data for *in vitro* loading within the *in vivo* range, as in the tests by Burr (1998) at 2700 με.

2.1. Experimental tests

New test data were obtained for bovine bone at a stress range of 70 MPa. In this work we used the same protocol as described previously (O' Brien et al., 2003), the only difference being the stress level. Ten cylindrical samples of bovine bone were obtained using a coring device, the longitudinal axis of the sample corresponding to the bone's axis. The diameter of the sample was reduced in a central portion and the ends were inserted in metal caps to facilitate attachment to a servo-hydraulic testing machine. Ranges for physiological frequencies are given between 0.5 and 3 Hz, in the present work cyclic loading was carried out in compression at a frequency of 3 Hz; the ratio of the minimum stress to the maximum stress was 0.1. Tests performed by researchers such as the ones published by Burr (1998), used one single dye, for which it was necessary to test two separate groups of bones: one to study microdamage developed *in vivo*, the other to study microdamage developed under external fatigue loads. The tests performed in the current work used three different coloured dyes, to label microcracks in the same specimens at three stages: the start of the test (i.e. *in vivo* cracks); after 50,000 cycles and after fracture or one million cycles, whichever happened first. The reason for selecting 50,000 cycles for the second dye was to detect microcracks which formed after a relatively small number of cycles, compared to the number of cycles to failure, since it has previously been observed that significant number of cracks form in this early stage (O' Brien et al. 2003).

The dimensions of the samples used in these tests (gauge length, reduced diameter, radius of curvature at transition region, and grip region length) are shown in Fig. 1.

2.2. Simulation of microcrack distribution

In addition to obtaining experimental data on microcrack length distributions, we also attempted to simulate this data, in two different ways. In both cases the underlying assumption was that microcracks initiate in the so-called interstitial bone (i.e. in those regions of bone which lie outside the osteons) and that cracks tend to stop growing when their tips reach the cement lines surrounding osteons. Fig. 2(a) illustrates cement lines stopping the growth of a microcrack (Griffin and Gibeling, 1997); (b) and a crack passing close to an osteon tending to be attracted towards the cement line, in a sample of the bovine bone tests from the current work.

Given sufficient time and/or stress, these cracks may continue to elongate, but our previous work (O' Brien, 2005; O' Brien et al., 2007) and that of others (Schaffler et al., 1995) has shown that 80%–90% of all cracks become dormant at an early stage. Thus we reasoned that an approximate simulation of the distribution of microcrack lengths, at least for the great majority of cracks, might

Table 1
Summary of data sources.

Dataset	Bone type	Stress	Number of cycles	Reference
1	Canine radius	*In vivo*	*In vivo*	Gellasch and Kalscheur (2002)
2	Canine femur	*In vivo*	*In vivo*	Burr (1998)
3	Canine femur	2700 με	Approx. 426,000 cycles	Burr (1998)
4	Ovine rib	*In vivo*	*In vivo*	Khan (2010)
5	Bovine tibia	*In vivo*	*In vivo*	O' Brien et al. (2003); Present study
6	Bovine tibia	70 MPa	50,000 Cycles	Present study
7	Bovine tibia	80 MPa	50,000 Cycles	O' Brien et al. (2003)
8	Bovine tibia	70 MPa	Million cycles non-fractured	Present study
9	Bovine tibia	70 MPa	Fracture av. 159,700 cycles	Present study
10	Bovine tibia	80 MPa	Fracture av. 88,000 cycles	O' Brien et al. (2003)