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A fatigue microcrack alters fluid velocities in a computational model of interstitial fluid flow in cortical bone

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Abstract

Targeted remodeling is activated by fatigue microcracks and plays an important role in maintaining bone integrity. It is widely believed that fluid flow-induced shear stress plays a major role in modulating the mechanotransduction process. Therefore, it is likely that fluid flow-induced shear stress plays a major role in the initiation of the repair of fatigue damage. Since no in vivo measurements of fluid flow within bone exist, computational and mathematical models must be employed to investigate the fluid flow field and the shear stress occurring within cortical bone. We developed a computational fluid dynamic model of cortical bone to examine the effect of a fatigue microcrack on the fluid flow field. Our results indicate that there are alterations in the fluid flow field as far as 150 μm away from the crack, and that at distances farther than this, the fluid flow field is similar to the fluid flow field of intact bone. Through the crack and immediately above and below it, the fluid velocity is higher, while at the lateral edges it is lower than that calculated for the intact model, with a maximum change of 29%. Our results suggest that the presence of a fatigue microcrack can alter the shear stress in regions near the crack. These alterations in shear stress have the potential to significantly alter mechanotransduction and may play a role in the initiation of the repair of fatigue microcracks.

Keywords: Fatigue microcracks; Targeted remodeling; Interstitial fluid flow; Computational fluid dynamics; Mechanotransduction

1. Introduction

Bone undergoes continuous remodeling to maintain its structural integrity (Raisz, 1999). Targeted remodeling is activated by and repairs fatigue microdamage while nontargeted remodeling serves purposes such as calcium homeostasis (Mori and Burr, 1993; Burr, 2002). It has been shown experimentally that as much as 30% of all remodeling is targeted remodeling (Mori and Burr, 1993), and theoretically that all remodeling could be initiated by fatigue microcracks (Martin, 2002). In vivo, microcracks develop as a result of cyclic bone loading during normal daily activity (Schaffler et al., 1995; Donahue et al., 2000). The accumulation of microcracks may contribute to the increased skeletal fragility associated with aging and may increase the risk of fragility fracture in older women (Burr et al., 1997). Discovering the mechanisms responsible for the repair of fatigue microdamage is important because fragility fractures have a huge clinical impact and economical burden.

Fatigue fractures (i.e. stress fractures) may also occur as a result of an accumulation and coalescence of microcracks (Muir and Ruaux-mason, 2000), but the repair of microcracks by remodeling may prevent fracture if the rate of accumulation does not exceed

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the rate of repair (Burr et al., 1985; Martin, 1992). Fatigue microcracks are associated with resorption spaces at least four to six times more often than predicted by chance alone (Burr, 1993; Burr, 2002). The most compelling evidence for a cause and effect relationship between microcracks and remodeling has been demonstrated in rats (Bentolila et al., 1998). While neither microcracks nor osteons are normally present in rat cortical bone, when microdamage within the cortex is mechanically induced, intracortical remodeling is activated. This intracortical remodeling is not random but rather it is directed towards regions of bone microdamage and altered osteocyte morphology (Bentolila et al., 1998). Verborgt et al. (1999) demonstrated that fatigue microdamage induced by mechanical loading causes osteocyte apoptosis to occur in a highly specific association with microdamage, which subsequently activates remodeling. Furthermore, it has been demonstrated that if remodeling activation is decreased by 68%, microdamage increases as much as 322% (Mashiba et al., 2000).

If microcracks act as a stimulus to initiate targeted remodeling, then what is the mechanism? It seems likely that the presence of a fatigue microcrack could alter lacuno-canalicular fluid flow, which would alter osteocyte shear stress and nutrient transport. Altered shear stress may activate the mechanotransduction signaling pathways which mediate targeted remodeling. It has been shown that osteoclastic resorption of fatigue-damaged bone coincides with regions of osteocyte apoptosis (Verborgt et al., 1999). Additionally, it has been demonstrated that in regions of bone that experience very low levels of physiological strain that the number of apoptotic osteocytes increases significantly, in comparison to regions of bone that experience high physiological levels of strain (Noble et al., 2003). Fluid flow is affected by changes in strain (Biot, 1941; Cowin, 1999). However, it is currently impossible to directly measure fluid flow velocities and shear stresses within the lacuno-canalicular system (Knothe Tate and Knothe, 2000). Therefore, it is necessary to use mathematical or computational modeling (Steck et al., 2000).

A number of models have been created to study fluid flow in bone (Dillaman et al., 1991; Weinbaum et al., 1994; Cowin et al., 1995; Mak et al., 1997; Wang et al., 1999; Srinivasan and Gross, 2000; Steck et al., 2000; Tami et al., 2002; Burger et al., 2003; Steck et al., 2003). Many of these models use a porous media approach and assume that Darcy's Law is valid within the porous structure of bone. This is beneficial because the size scale of such models is comparable to the size scale of a whole bone. Since mechanical loading of bone creates the pressure gradients that drive fluid through the porous spaces of bone tissue, this is a desirable modeling approach (Knothe Tate et al., 1998; Steck et al., 1998).

It is believed that load-induced fluid flow in the porous spaces of bone plays a key role in remodeling by enhancing molecular transport (Piekarski and Munro, 1977), generating streaming potentials (Turner et al., 1994) or by inducing bone cell membrane shear stress (Turner et al., 1994; Weinbaum et al., 1994; Cowin et al., 1995). Therefore, it is reasonable to postulate that alterations in lacuno-canalicular fluid flow, caused by microdamage, activate the signaling cascade that initiates targeted bone remodeling. In fact, it has been demonstrated computationally that the presence of a fatigue microcrack significantly alters nutrient transport in the lacuno-canalicular system (Tami et al., 2002). In the present study, computational fluid dynamic models of cortical bone were developed for intact bone and bone containing a fatigue microcrack. The objective of this study was to determine how a fatigue microcrack affects the fluid flow field for physiological levels of loading.

2. Methods

We modeled $1\,\text{mm} \times 1\,\text{mm}$ transverse sections of cortical bone from the human second metatarsal bone using computational fluid dynamics (CFD) and the commercial software STARCD (CD Adapco Group, Melville, NY). Two CFD models were created, one for an intact geometry and a second with a central defect, the size and shape of a fatigue microcrack. A single microcrack was used because the density of microcracks in the second metatarsal is $0.24 \pm 0.21\,\#/\text{mm}^2$ (Donahue et al., 2000). Preliminary computational models using a large defect indicated that any changes in the flow field would be captured by the $1\,\text{mm} \times 1\,\text{mm}$ domain.

Microcracks are approximately elliptical with a length to width ratio of 10:1 (O'Brien et al., 2000). The average length of a fatigue microcrack in the human second metatarsal is $75.91 \pm 18.81\,\mu\text{m}$ (Donahue et al., 2000). Therefore, we modeled a $100\,\mu\text{m} \times 10\,\mu\text{m}$ microcrack to represent the upper limit of in vivo cracks. The modeled microcrack had an idealized shape that quite accurately depicted the real shape and size of an in vivo fatigue microcrack (Fig. 1). Two-dimensional models of cortical bone, without cellular material, were created by representing the lacuno-canalicular system as an idealized porous media with a porosity of 0.05 (Zhang et al., 1998). Haversian canals were included because their size (e.g., $30\,\mu\text{m}$ diameter) is the same size scale of the microcrack (Wang et al., 2000). The average density of Haversian canals is approximately $15/\text{mm}^2$ (Martin et al., 1980). To maintain symmetry in our model, eight Haversian canals were included (Fig. 1C) as $30\,\mu\text{m}$ diameter circles with void centers and a $1\,\mu\text{m}$ ring at the outer surface with a porosity of 0.025 representing penetrating canaliculi (Zhang et al., 1998). The