Osteoporotic bone fracture healing under the locking compression plate system

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Abstract

Osteoporosis is highly prevalent and a costly disease predicted to affect 1,555 million worldwide by 2050, and the total cost of osteoporotic fractures worldwide could reach US$131 billion by 2025. These statistics clearly affirm the significant economic burden of osteoporotic fractures to the community, and the need for the development of improved fracture treatments. Studies over the last decade reveal that, even though osteoporosis may not necessarily lead to non-union, it is associated with delayed fracture healing due to impaired mecho-regulation and angiogenesis in osteoporotic condition. Despite the advances in locking compression plate (LCP) technology, the operative treatment in osteoporotic fractures remains a challenge for an orthopaedic surgeon, often with unpredictable outcomes. Therefore, it becomes necessary to bridge the 'information gap' between osteoporosis and its effect on fracture healing, and so enables healing progression prediction under different fracture geometries and fixation configurations. By using a computational model of fracture healing, this paper demonstrates that fracture healing can be significantly delayed due to impaired mechano-regulation as a result of osteoporosis, and the impact of osteoporosis on fracture healing can be mitigated by adjusting the configuration of the LCP system to allow a certain degree of interfragmentary movement (IFM) without compromising overall fixation stability.

Keywords: Osteoporosis; Fracture healing; Interfragmentary movements (IFM); Locking compression plate (LCP).

Introduction

Osteoporotic fractures lead to chronic pain, disability, loss of independence and even premature death. The total cost of fracture management in community health programs, aids and appliances, and indirect costs, such as lost earnings, is projected to rise to US$131 billion worldwide by 2050 (Harvey et al., 2010; Watts et al., 2013). Osteoporosis is associated with delayed fracture healing (Augat et al., 2005; Namkung-Matthai et al., 2001), even though it is not a risk factor for non-union (Wunnik et al., 2011). Although it still remains an open question whether fracture repair is impaired in osteoporosis, the mechanical and biological factors involved in the healing process are certainly affected (Augat et al., 2005; Nikolaou et al., 2009). Firstly the reduction in number of mesenchymal stem cells and their impaired response to mechanical stimuli in osteoporotic condition may lead to a delayed fracture healing. Secondly osteoporosis related the impaired growth factor expression and abnormalities in endothelial cells could result in impair angiogenesis progression. Current therapies for osteoporotic fractures focus on prevention, however, little emphasis has been given to the study of the fracture healing process itself in osteoporotic bone.

The initial phase of healing is especially sensitive to mechanical conditions and influences the course of healing (Klein et al., 2003). It is widely believed that callus cell differentiation and proliferation are closely regulated by the magnitude of the so-called 'stimulus index (S)', which is determined by the octahedral shear strain and the interstitial flow velocity within a fracture callus. Mesenchymal stem cells differentiate into chondrocytes, osteoblasts and fibroblasts depending on their biomechnical microenvironment. However, fracture healing in osteoporotic bone may display

an impaired response to these mechanical stimuli (Sterck et al., 1998) due to the presence of fewer mesenchymal stem cells in osteoporotic bone, and a relatively lower proliferative response (Bergman et al., 1996; Giannoudis and Schneider, 2006). For example, an osteoporotic rat model showed a 40% reduction in the cross-sectional area of callus and a 23% reduction in bone mineral density in healing rate femurs (Namkung-Matthai et al., 2001).

The mechanical microenvironment in a fracture callus is greatly influenced by the IFM which is largely dependent on the mechanical stiffness of a LCP. The stiffness of an osteoporotic fracture fixation construct, such as the locking compression plate (LCP) system, has normally to be increased as osteoporosis decreases the mechanical properties of bone. However, an overly stiff fixation construct may lead to impaired IFM at the fracture site which inhibits callus formation, and may lead to potential delayed healing or non-union (Gardner et al., 2010). Clinically, the flexibility of LCP could be enhanced by adjusting the working length (WL), bone-plate (BPD) and number of screws (Claes, 2011). However, the effect of the flexibility of LCP on osteoporotic bone healing has not been fully investigated. The problem becomes further complicated as fixation failure occurs as a consequence of reduced bone density (Barrios et al., 1993).

Thus, the key questions are:

1. How is the mechao-regulation altered in osteoporosis?
2. How can the fixation design be strategically modified to achieve improved fracture healing outcomes in osteoporosis?

To address these questions, the development to computational models for osteoporotic fracture healing becomes necessary.

Methods

Error! Reference source not found. Figure 1 shows the impact of both osteoporosis and fixation configuration on healing outcomes. Fracture healing is a time-dependent process which is closely regulated by the changes in mechanical microenvironment of fracture site as a result of a change of interfragmentary motion at fracture site as healing progresses. We have recently brought together our previously developed poroelastic large deformation model of biological soft tissues and tissue/cell-level mechano-regulation model of fracture callus to gain a new insight into the early stage bone healing under different configurations of LCP (Miramini et al., 2014; Miramini et al., 2015; Zhang, 2015; Zhang et al., 2013; Zhang et al., 2012). The mechanical behavior of fracture callus is described by using a consolidation approach (Zhang et al., 2007, 2008; Zhang et al., 2009; Zhang et al., 2010) which treats callus as a fluid-saturated porous medium comprising an intrinsically solid phase (i.e. collagen-proteoglycan matrix) and a fluid phase. Mass conservation equations are written for each phase, while empirical laws (e.g. Darcy's law) are used to describe relative velocity of each phase. Finally, momentum conservation laws can capture the interaction of the mechanical

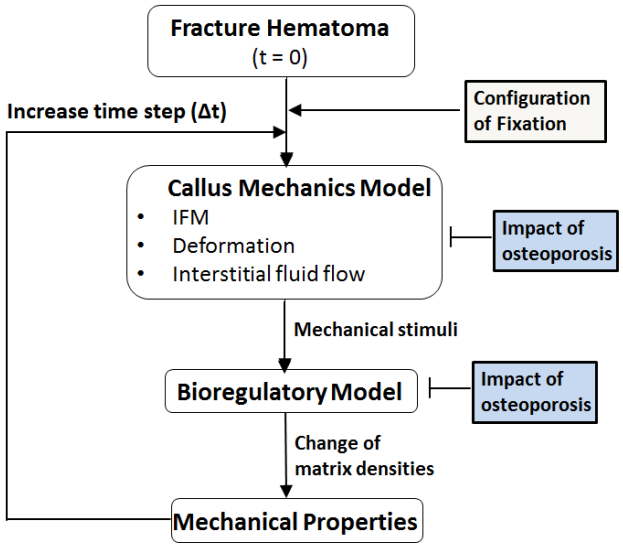

Figure 1 The schematic diagram shows the impact of osteoporosis and fixation configuration on healing outcomes.

quantities in each component. The model can be easily further extended by incorporating the impact of osteoporosis on fracture healing.

The framework of fracture healing model is shown in Figure 2. Our developed model allows the high resolution 3D modelling of a tibia containing a fracture from the 2D computed tomography (CT) image data (Miramini et al., 2015; Zhang, 2015; Zhang et al., 2013; Zhang et al., 2012). The 3D meshed part of the fractured tibia is then exported into finite element applications. The model enables the determination of the change of mechano-regulation distribution profiles (e.g. interstitial fluid flow and deformation) in fracture callus arising from external mechanical loading. Finally, the model predicts the tissue development regulated by callus cells that respond to their mechanical microenvironments. Furthermore, our developed model is capable of taking into consideration the fracture conditions (e.g. size, shape and position), fixation treatment selection, and loading regimes resulting from patient-specific physiological movement. In this paper, our developed model is implemented to investigate the effect of impaired mechanical stimuli due to osteoporosis on the healing outcomes at early stage of healing.

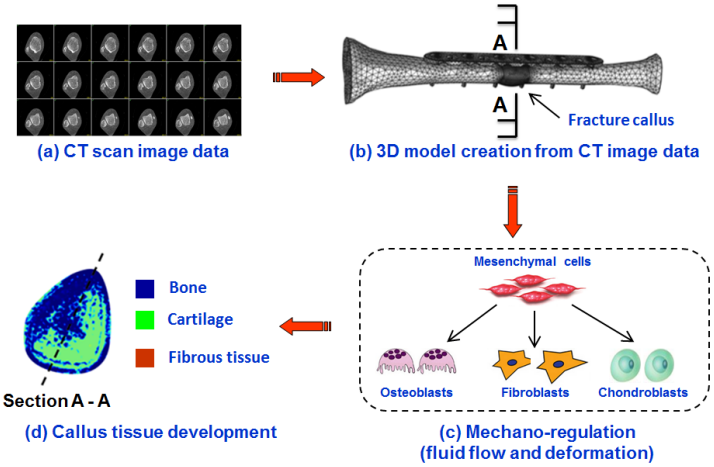

Figure 2 The framework of fracture healing model. (a) Computed tomography (CT) image data. (b) 3D model created from the CT images. (c) In vivo, cells in fracture callus regulate the healing processes by responding to changes in their mechanical microenvironments. (d) Mechanical stimuli mediated tissue differentiation.

Results and Discussion

As shown in Figure 3, the effect of 25%, 50% and 75% impaired mechanical response of callus cells resulting from osteoporosis on tissue differentiation outcomes is investigated respectively. The results show that at the same time point after surgery, the impaired mechanical stimuli due to osteoporosis could potentially delay the healing process by inhibiting cartilage tissue development at the early stage of healing. However, by allowing certain degree of flexibility of LCP system without compromising the overall stability of the construct (i.e. increasing BPD from 0mm to 2mm), the impact of osteoporosis on fracture healing can be significantly mitigated.

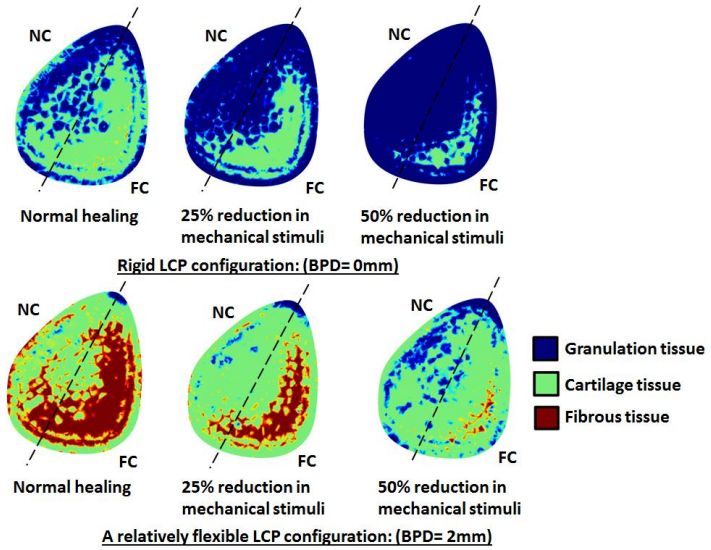

Figure 3 The investigation of the effects of impaired mechano-regulation as a result of osteoporosis and the flexibility of LCP configuration on tissue differentiation at early stage of fracture healing.

Conclusions

This paper presents an osteoporotic fracture healing computational model, which could bridge the 'information gap' between osteoporosis and its effect on fracture healing, and so enable healing progression predictions under different fracture geometries and fixation configurations. The developed model will allow orthopaedic surgeons to design patient-specific surgical solutions by establishing a rigorous scientific relationship between the configuration of the fixation system and the biological processes of healing in patients with osteoporosis, and thereby achieve optimal fracture healing outcomes.

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