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Influence of fracture geometry on bone healing under locking plate fixations: A comparison between oblique and transverse tibial fractures

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ABSTRACT

Mechano-regulation plays a crucial role in bone healing and involves complex cellular events. In this study, we investigate the change of mechanical microenvironment of stem cells within early fracture callus as a result of the change of fracture obliquity, gap size and fixation configuration using mechanical testing in conjunction with computational modelling. The research outcomes show that angle of obliquity (θ) has significant effects on interfragmentary movement (IFM) which influences mechanical microenvironment of the callus cells. Axial IFM at near cortex of fracture decreases with θ, while shear IFM significantly increases with θ. While a large θ can increase shear IFM by four-fold compared to transverse fracture, it also result in the tension–stress effect at near cortex of fracture callus. In addition, mechanical stimuli for cell differentiation within the callus are found to be strongly negatively correlated to angle of obliquity and gap size. It is also shown that a relatively flexible fixation could enhance callus formation in presence of a large gap but could lead to excessive callus strain and interstitial fluid flow when a small transverse fracture gap is present. In conclusion, there appears to be an optimal fixation configuration for a given angle of obliquity and gap size.

Introduction

Oblique fracture is one of the most common fracture types among all the long bone fractures, and approximately 30–40% of tibial shaft fractures are oblique [1,2]. Due to the oblique geometry, these fractures are especially susceptible to delayed healing or non-union [2–4]. Although it was suggested that the large bone fragment surface area of an oblique fracture could improve bone healing capacity, the special geometry of oblique fractures could still result in delayed healing or non-union [3].

Aro et al. [3] compared fracture healing between transverse and oblique osteotomy in canine tibia stabilized by external fixation. The right and left tibias of eleven adult dogs were randomly undergone transverse and 60° oblique osteotomy, respectively, and then fixed for healing by the same type of external fixation. The experimental results showed that, at 60 days post-surgery, the bending stiffness of the oblique fractures was 76.8% of that of the transverse fractures. Further, the oblique fractures apparently resulted in delayed healing in comparison to the transverse ones, e.g. the bending stiffness of an oblique fracture generally required 90 days to reach that of an intact bone, whereas a transverse fracture healed much faster taking 60 days to regain full bending stiffness.

The excessive shear movement at the fracture site has been identified as an important determinant of instability in oblique fractures, leading ultimately to impaired angiogenesis which prevents normal healing process [4–9]. It was suggested that as angiogenesis is very dependent on the fracture site stability, the excessive shear IFM may impede the longitudinal development of blood vessels in the fracture site, thereby leading to impaired ossification of the callus tissue [9]. A recent computational study has confirmed the negative effect of shear IFM on bone healing [10].

In recent years, application of locking plate fixation has become increasingly popular in clinical practice for internal fixation of fractures [11] and has been particularly promising for the fixation of osteoporotic fractures [11–13]. The locking plate fixation bridges the fracture gap and allows a certain degree of IFM to promote callus formation and indirect bone healing [14]. The clinical application of locking plate fixation requires careful pre-operation planning to maximize its effectiveness [15]. However, the scientific

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basis of this pre-operation planning, especially its effect on oblique fractures, has not been well understood to date.

We have recently developed a validated computational model to simulate mechanical microenvironment of the fracture callus under locking plate fixation for transverse fractures [16–19]. Through application of the theory of porous media [20] and the mechanoregulation theory of Prendergast et al. [21], the model has the capability of predicting the early stage of bone healing for a transverse fracture under various configurations of locking plate fixation [19] via quantification of both tissue strain and interstitial fluid flow which are two important mechanical stimuli for callus cell differentiation. Although it is widely known that mechanical microenvironment of early callus cells can be influenced by fracture fixation, fracture geometry as well as applied loading [22–25], the influence of fracture obliquity on mechanical microenvironment of bone healing of fractures stabilized by locking plate is still unclear.

By using experimental testing in conjunction with computational modelling, in this study, we aimed to investigate the changes in the mechanical microenvironment of fracture callus cells and subsequently cell differentiation, resulting from the changes of the angle of obliquity, fracture gap size and configuration of locking plate fixation. The focus of this study was on the early stage of bone healing as it has been demonstrated that the mechanical condition at this stage is critically important and can influence the entire healing process [22–25]. It was demonstrated that during the early stage of healing, mesenchymal stem cells and osteo-chondroprogenitor cell in the fracture callus commit to chondrogenic or osteogenic fate [24] and consequently they are especially sensitive to their mechanical microenvironment [23].

2. Material and methods

To achieve the study aim, firstly the axial and shear IFM of surrogate fractures with different angles of obliquity stabilized by locking plate fixation were measured through mechanical testing involving an INSTRON testing machine and 3D optical measurement system (ARAMIS). Then, the effect of experimentally observed IFM on mechanical microenvironment of fracture callus was investigated using our computational model of fracture healing.

2.1. Mechanical testing

Twenty adult human tibia surrogate specimens manufactured by Synbone (Malans, Switzerland) were used in the mechanical experiment. Mechanical testing using Synbone tibia surrogate are widely used to investigate biomechanical behaviour of different fracture fixation methods [26,27]. The surrogates were made of specially formulated polyurethane foam comprising of inner cancellous bone and outer shell of cortical bone which provide similar geometrical and mechanical properties to real adult human tibia with around 1500 MPa average compressive Young's modulus and 0.25 Poisson's ratio. The purpose of using surrogate bone tibia instead of cadaver specimens was to eliminate inter-specimen variability in the analysis of the influence of fracture obliquity on the fracture IFM. Standard stainless steel 4.5 mm broad Locking Compression Plate (LCP) with locking screws manufactured and provided by DePuy Synthes (Oberdorf, Switzerland) were applied anteromedially on the tibia surrogate diaphysis. The plates were 206 mm long, 17.5 mm wide and 5.2 mm thick with 11 holes, while the locking screws were 40 mm long with 4.5 mm core diameter. Based on the guideline proposed by Gautier and Sommer [28], the screw holes were produced by a drill bit of Ø4.3 mm and the screws were placed in the first, third and fifth holes from the fracture site and were tightened to 4 Nm. In addition, a bone-plate distance (BPD) of 2 mm was adjusted on the fracture model by temporary spacers during specimen preparation. After application of locking plate fixations on the surrogates, fractures with different angles of obliquity (i.e. $\theta = 0°$, 15°, 30° and 45°) were created on the surrogates. Figs. 1 and 2a illustrate mechanical testing set-up and geometry of the fracture model respectively.

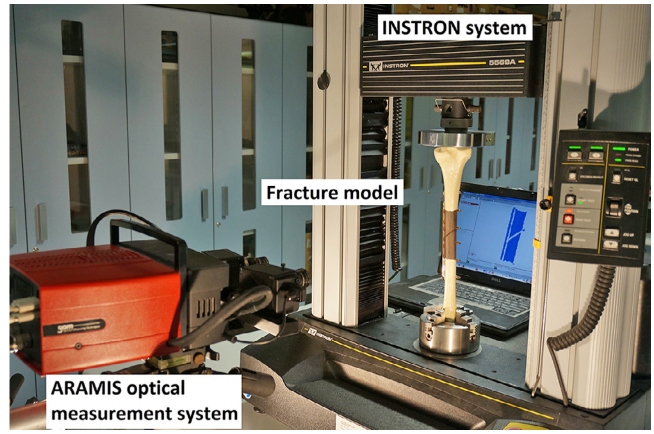

Fig 1. Mechanical testing of surrogate tibia bone specimens using INSTRON testing machine and 3D optical measurement system (ARAMIS).

Table 1
Experimental groups used in the mechanical testing.

Group	Angle of obliquity (θ)	Sample size
C1 (control)	0°	5
C2	15°	5
C3	30°	5
C4	45°	5

The fracture models were tested under axial compression by a material testing system (INSTRON 5569A, Canton, Massachusetts). The distal fragment of the tibia was fixed in a lathe chuck and the axial compressive load was applied on the tibia intercondylar eminence to allow free rotation (Fig. 1). This set-up simulates the physiological loading conditions applied on tibia through knee and ankle [29,30]. As illustrated in Table 1, four groups of five specimens were tested and an axial compressive load of 100, 150 and 200 N in 0.5 s was applied to the specimens. These loading conditions represent the partial weight bearing situation following surgical operation [31]. As shown in Fig. 2a, the axial IFM (i.e. IFM component in z-direction which is normal to the fracture line) and the shear IFM (i.e. IFM component in x-direction which is parallel to the fracture line) were measured using 3D optical measurement system ARAMIS (GOM, Braunschweig, Germany).

A two-factor ANOVA test was conducted to analyse the effect of angle of obliquity and applied loading, and their interaction on axial and shear IFM. In addition, for each magnitude of loading, the axial and shear IFMs were cross-compared using unpaired t-test to detect differences resulting from different angles of obliquity. A significance level of 5% was used in the statistical analysis.

Our pilot study conducted before the main experiments indicted that a sample size of 5 in each group is required to provide a statistical power of 89% with a significance level of 5% to detect significant differences resulting from different angles of obliquity and magnitudes of applied loading. The statistical analysis was performed using MATLAB (R2010, The MathWorks, Inc., Natick, MA, USA).

2.2. Computational modelling of early stage of healing

In this research step, the influence of IFMs (observed in the mechanical testing of Section 2.1) on the early stage of healing was