

## The effects of flexible fixation on early stage bone fracture healing

**\*\*L. Zhang<sup>1</sup>, S. Miramini<sup>1</sup>, P. Mendis<sup>1</sup>, M. Richardson<sup>2</sup>, M. Pirpiris<sup>2</sup> and A. Oloyede<sup>3</sup>**

<sup>1</sup> Department of Infrastructure Engineering, The University of Melbourne, Australia.

<sup>2</sup> The Epworth Hospital, Richmond, Australia.

<sup>3</sup> Science and Engineering Faculty, Queensland University of Technology, Australia

\*Corresponding author: [lih Zhang@unimelb.edu.au](mailto:lih Zhang@unimelb.edu.au)

### Abstract

The mechanical microenvironment at a fracture site could potentially influence the outcomes of bone fracture healing. It is known that, should the fixation construct be too stiff, or the gap between the fracture ends be too large, bones are less likely to heal. Flexible fixation or so-called “biological fixation” has been shown to encourage the formation of fracture callus, and therefore result in better healing outcomes. However, till date the nature of the relationship between the degree of mechanical stability provided by a flexible fixation and optimal healing fracture healing outcomes has not been fully understood. This paper presents a computational model that can predict healing outcomes from early stage healing data under various fixation configurations. The results of the simulations demonstrate that the change of mechanical microenvironment of fracture site resulting from the different fixation configurations is of importance for the healing outcomes.

**Keywords:** bone fracture healing; locking compression plate (LCP); interfragmentary movements (IFM); mechanical microenvironment; computational modelling.

### Introduction

The flexibility of internal fixation systems affects the formation of fracture callus as a result of interfragmentary strain (IFS) at fracture site (Zhang et al. 2012). It has been demonstrated that the initial phase of healing is especially sensitive to IFS and influences the ultimate healing outcomes as the initial interfragmentary movements are higher at early stage of healing after surgery (Carter et al. 1988; Klein et al. 2003). For example, it has been established that there is a strong correlation between hydrostatic fluid pressure and tissue differentiation in the initial stages of fracture healing (Carter et al. 1988), and that bone healing is influenced by the stability of initial shear fixation (Chell et al. 1995). However, despite several research efforts around the world over the last decades, there still remains a significant gap in our understanding of the relationships between mechanical stability conditions and the biology of bone fracture healing processes (Perren 2002b).

Apparently, soft callus formation is especially important for the stabilization of the fracture site through the stages of healing, and if not properly formed could result in malfunctioning bone segment union. To improve the healing outcomes and avoid the risks of delayed union and non-union, various types of fixation have been developed in the last decades. Standard fixation plates which mainly focus on mechanical stability (so called “absolutely stability”) through the compression of standard plates against underlying bone using normal screws, could lead to delayed healing, damage to blood supply of fracture site and underlying periosteum (Szypryt and Forward 2009). With the development of locking plate, which acts as an internal splint and load sparing device, the compression between plate and bone becomes unnecessary. Particularly, the application of locking plate in osteoporotic patient reduces the risks of fixation failure resulting from the pull out of screws (Szypryt and Forward 2009). In addition, the core diameter of a locking head screw (LHS) is normally larger than that of a standard cortical screw, and so could provide much greater strength in bending (200%) and shear (100%). The purpose of locking plate is to promote formation of fracture callus via allowing a certain degree of IFM at the fracture gap without compromising the

overall mechanical stability of the fracture site (Perren 2002a). However, as the mechanical properties of widely used locking plate material (*e.g.* stainless steel and titanium) are normally much higher than that of bone, standard locking plate might still suppress interfragmentary movements required for indirect bone healing (Claes et al. 2011; Henderson et al. 2008; Lujan et al. 2010b). Further, although the locking plate allows some IFM to help simulate callus formation, the generated IFM is not uniformly distributed across the fracture site (*i.e.*, much smaller IFM at near cortex in comparison to that at far cortex), and this spatially dependent IFM could lead to asymmetric tissue distribution within the callus, and ultimately delayed healing (Bottlang et al. 2010; Lujan et al. 2010b).

Several attempts have been made to further improve flexibility of locking plates with the aim of simulating the formation of callus. For example, recent studies have been increasingly focused on the development of innovative plate materials with material mechanical properties more similar to bone such as composite polymers (JH and SH 2007; Kim et al. 2010; Zdero and Bougherara 2010) and metal foams (Rabiei 2010; Rabiei 2012). However this new concept is still in its infancy and needs more biomechanical and clinical investigations in order to be widely accepted by the orthopaedic community. Clinically, the flexibility of the locking plates could be enhanced by adjusting the working length (WL), bone-plate distance (BPD) and number of screws (Ahmad et al. 2007; Claes 2011; Hak et al. 2010; Miller and Goswami 2007; Stoffel et al. 2003), however the limitations of these surgical techniques lie in their incapability of solving the problem of the significant difference between the IFM at the near and far cortex zones of the callus which leads to asymmetric callus formation and possibly delayed healing and non-union (Bottlang et al. 2010; Claes 2011; Lujan et al. 2010b). To tackle this issue, the dynamic locking screw (DLS) was recently developed with the aim of increasing the IFM in the near cortex zone, and ultimately uniform callus formation (Bottlang et al. 2009; Bottlang and Feist 2011; Bottlang et al. 2010; Döbele et al. 2010; Doornink et al. 2011; Gardner et al. 2009; Gardner et al. 2010; Plecko et al. 2012; Sellei et al. 2011). Different from LHS, DLS consists of an outer sleeve attached to the bone and an inner pin with reduced diameter at the near cortex resulting in the increase of the IFM on the near cortex side, and consequently enhancing callus formation in this area (Bottlang et al. 2010; Plecko et al. 2012; Sellei et al. 2011). However, none of these techniques has proved adequate till date due to the lack of fundamental understanding of the relationship between mechanical stability conditions and the biology of bone fracture healing process. Therefore, the objective of this paper is to develop a computational model that facilitates the understanding of the relationships between the change in the mechanical environment of a fracture site and varying fixation configurations of a locking plate system.

## Methods

After surgical installation of internal fixation, the fracture callus is developed within the fracture gap by filling with granulation tissue during the first several days of healing during which the biomechanical condition is of critical importance for the ultimate healing outcomes (Epari et al. 2006; Klein 2003; Thompson et al. 2002). At this stage, callus could be treated as a porous fluid saturated material (González-Torres et al. 2010) that could be modeled by the theory of porous media which is commonly used to study the mechanical behavior of biological soft tissues (*e.g.* cartilage and brain) (Oloyede and Broom 1991; Oloyede and Broom 1994; Zhang et al. 2007; Zhang et al. 2008; Zhang et al. 2009). Considering a particular constituent of a fluid-filled soft biological tissue (*e.g.* callus) occupies a domain  $\Omega_0^\alpha$ , *i.e.* solid phase ( $\alpha = s$ ) or fluid phase ( $\alpha = f$ ). The time-dependent position of the particle in the current Eulerian configuration  $\Omega$ , is given by

$$x(X^\alpha, t) = X^\alpha + u^\alpha(X^\alpha, t) \quad (1)$$

where  $u^\alpha$  is the  $\alpha$ -constituent displacement. The volume fraction of solid and fluid phase may be defined respectively as

$$\phi^s + \phi^f = 1 \quad (2)$$

Assuming intrinsically incompressible constituents, the Cauchy stress tensors of the solid and fluid phases are defined as

$$\boldsymbol{\sigma}^s = -\phi^s p \mathbf{I} + \boldsymbol{\sigma}_E^s \quad (3)$$

$$\boldsymbol{\sigma}^f = -\phi^f p \mathbf{I} \quad (4)$$

where  $\boldsymbol{\sigma}_E^s$  is the elastic stress resulting from solid deformation and  $\mathbf{I}$  is the identity tensor. If the solid constituent can be treated as hyperelastic, then

$$\boldsymbol{\sigma}_E^s = \frac{1}{J^s} \mathbf{F}^s \bullet 2 \frac{\partial U(\mathbf{u}^s)}{\partial \mathbf{C}^s} \bullet \mathbf{F}^{sT} \quad (5)$$

where  $U(\mathbf{u}^s)$  is the Helmholtz energy per unit reference volume stored in the solid,  $\mathbf{F}^s$  is the deformation gradient of the solid phase,  $\mathbf{C}^s = \mathbf{F}^{sT} \bullet \mathbf{F}^s$  is the right Cauchy-Green deformation tensor of the solid phase, and  $J^s = \det \mathbf{F}^s$  is the volume change of solid phase.

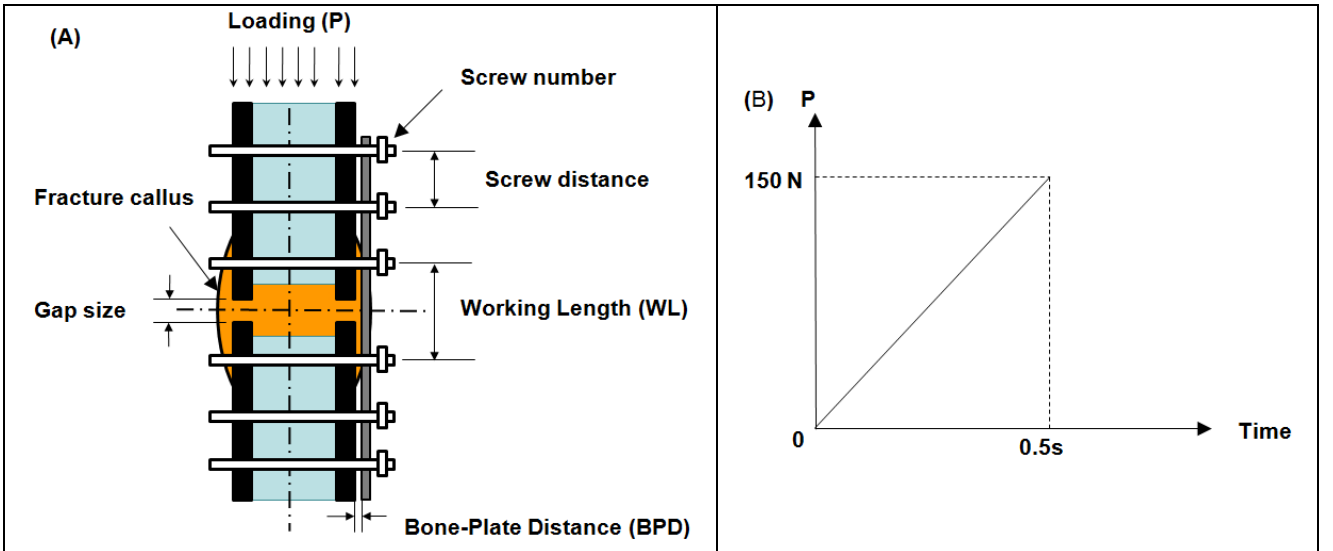
Ignoring the body and inertial forces, the momentum equation of the solid phase is given by

$$\nabla \bullet \boldsymbol{\sigma}^\alpha + \pi^\alpha = 0 \quad (6)$$

where  $\boldsymbol{\sigma}^\alpha$  is the Cauchy stress tensor for the  $\alpha$ -constituent,  $\pi^s$  and  $\pi^f$  are momentum exchange vectors describing the frictional interactions between the solid phase and fluid phase. That is,

$$\pi^s = -p \nabla \phi^f + (\phi^f)^2 \kappa^{-1} \bullet (\mathbf{v}^f - \mathbf{v}^s) \quad (7)$$

where  $\kappa$  is the symmetric Darcy permeability tensor.



**Figure 1** Fixation conditions of locking plate for computational modeling of bone fracture healing characteristics at early stage.

**Table 1 Parameters used in this study (Lacroix and Prendergast 2002; McCartney et al. 2005)**

	Young's modulus (MPa)	Poisson's Ratio	Porosity	Permeability (m <sup>4</sup> /Ns)	Fluid phase compression modulus (MPa)	Solid phase compression modulus (MPa)
Granulation Tissue	0.05	0.17	0.8	10 <sup>-14</sup>	2300	2300
Marrow	2	0.17	0.8	10 <sup>-14</sup>	2300	2300
Cortical Bone	20000	0.3	0.04	10 <sup>-17</sup>	2300	13920

This study will theoretically investigate the tissue development simulated by the change of mechanical microenvironment of the fracture site resulting from various locking plate conditions. **Error! Reference source not found.** is a schematic diagram of the fixation conditions of the locking plate used in our analysis, and the values of parameters used in this study are shown in Table 1. The fractured bone is subject to a time-dependent load ( $P$ ) applied over 0.5s simulating physiological walking load (approx. 20% of the normal body weight that a patient could withstand after surgery) (Goodship 1985).

#### *Mechanoregulation of bone healing*

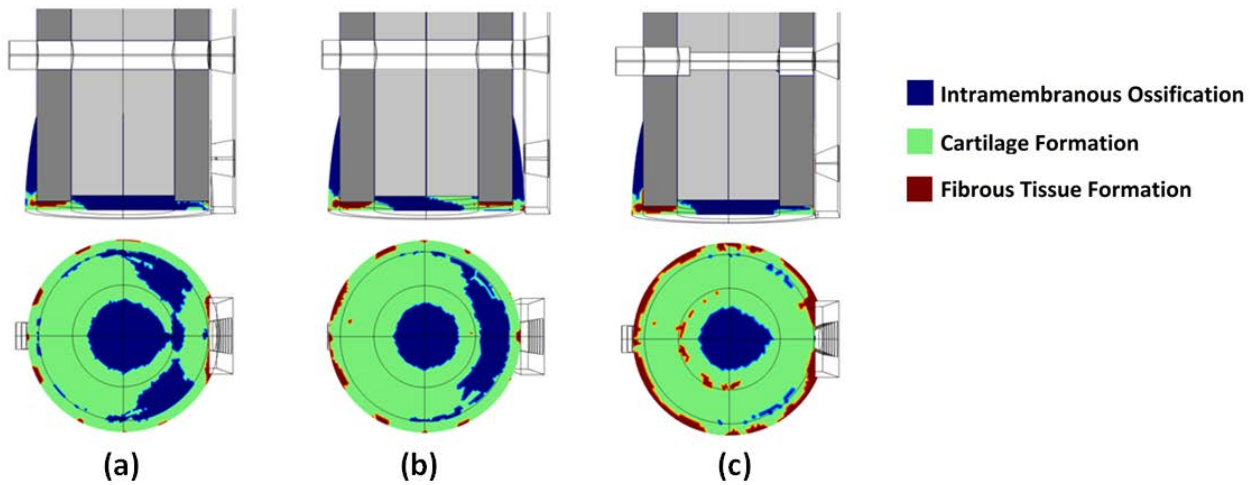
Assuming mesenchymal stem cell differentiation within fracture callus is simulated by the change of biomechanical microenvironment of cells, Prendergast et al suggested that the differentiation process of stem cells are governed by a so-called "Stimulus Index ( $S$ )", which is defined as (Prendergast et al. 2010)

$$S = \frac{\gamma}{a} + \frac{\nu}{b} \quad (8)$$

where  $a = 0.0375$ ,  $b = 3 \mu\text{m/s}$ ,  $\gamma$  is octahedral shear strain in callus and  $\nu$  is interstitial fluid flow within the callus. The values of  $\gamma$  and  $\nu$  can be obtained by solving the governing equations (3) – (7) using the commercial Finite Element software package COMSOL MULTIPHYSICS (2012). Therefore, the stem cells could exert spatially dependent differentiation behaviour within the callus depending on the magnitude of  $S$  in a particular region of callus. During the early stage of bone healing (*i.e.* first week after surgery), high magnitude of stimulus index ( $S > 3$ ) results in formation of fibrous tissue inside the callus, an intermediate  $S$  ( $1 < S < 3$ ) leads to cartilage tissue and bone formation via intramembranous ossification when the stimulus index  $S$  is small enough ( $S < 1$ ). During the next stages of bone healing, fibrous tissue is replaced by cartilage when  $1 < S < 3$  and the cartilage undergoes endochondral ossification and is replaced by woven bone when  $S < 1$ . The mechanoregulation theory proposed by Prendergast et al has been used in this study.

Synthes 4.5mm stainless steel Locking Compression Plate (224mm long, 17.5mm wide and 5.2mm thick with 12 locking holes) was used to compare the effects of various configurations of fixation using LHS, DLS and different BPDs on the healing outcomes. To promote indirect healing, intramembranous ossification is unfavourable at early stage of healing, in the meantime consistent and asymmetric callus formation is also of importance for ultimate healing outcomes (Lujan et al. 2010a).

## Results and Discussion



**Figure 2 Comparison of simulation results for callus formation in healing fracture sites under (a) LHS, BPD = 0mm (control); (b) LHS, BPD = 2mm; and (c) DLS, BPD = 2mm**

**Table 2 Tissue differentiation in the osteotomy gap**

Type	Intramembranous ossification	Cartilage formation	Fibrous tissue formation
(a)	37.10%	41.20%	21.70%
(b)	25.20%	44.70%	30.10%
(c)	15.10%	38.60%	46.30%

Figure 2 provides the prediction of tissue formation under (a) LHS, BPD = 0mm (control); (b) LHS, BPD = 2mm; and (c) DLS, BPD = 2mm, respectively. The amount of different tissues formation in the osteotomy gap (*i.e.* Intramembranous ossification, cartilage formation and fibrous tissue formation) is presented in Table 2. The simulation results demonstrate that under LHS, the increase of BPD by 2mm (Figure 2b) relative to the control (Figure 2a) has some beneficial effects in reducing intramembranous ossification by around 12%, however this increase of BPD is still unable to change the condition of asymmetrical tissue development within the callus due to the significant difference of interfragmentary strain between near and far cortex zones of the callus. In comparison to LHS, the use of DLS in combination with the increase of BPD produces the most encouraging results, *i.e.* reducing intramembranous ossification by more than 20%, and most importantly leading to more consistent and symmetric tissue development. The simulation results indicate that the application of DLS has substantial potential for improving bone healing outcomes.

## Conclusions

In this study, we have presented a computational model to predict bone fracture healing outcomes, demonstrating that the model could quantitatively describe tissue differentiation pattern in the early stages of fracture healing. Most importantly, the predicted results indicate that innovative fixation techniques such as DLS, could potentially lead to better healing outcomes via significantly reducing intramembranous ossification while promoting symmetric tissue development within the callus.

## Acknowledgments

The authors wish to acknowledge the support of Synthes Asia and Pacific and The Ian Potter Foundation, and The University of Melbourne.

## References

- (2012). "COMSOL Multiphysics." COMSOL Inc.
- Ahmad, M., Nanda, R., Bajwa, a. S., Candal-Couto, J., Green, S., and Hui, a. C. (2007). "Biomechanical testing of the locking compression plate: when does the distance between bone and implant significantly reduce construct stability?" *Injury*, 38, 358-64.
- Bottlang, M., Doornink, J., Fitzpatrick, D. C., and Madey, S. M. (2009). "Far cortical locking can reduce stiffness of locked plating constructs while retaining construct strength." *The Journal of bone and joint surgery. American volume*, 91, 1985-94.
- Bottlang, M., and Feist, F. (2011). "Biomechanics of far cortical locking." *Journal of orthopaedic trauma*, 25 Suppl 1, S21-8.
- Bottlang, M., Lesser, M., Koerber, J., Doornink, J., von Rechenberg, B., Augat, P., Fitzpatrick, D. C., Madey, S. M., and Marsh, J. L. (2010). "Far cortical locking can improve healing of fractures stabilized with locking plates." *The Journal of bone and joint surgery. American volume*, 92, 1652-60.
- Carter, D. R., Blenman, P. R., and Beaupré, G. S. (1988). "Correlations between mechanical stress history and tissue differentiation in initial fracture healing." *Journal of Orthopaedic Research*, 6(5), 736-748.
- Chell, H., Epari, D. R., Kassi, J. P., Bragulla, H., Bail, H. J., and Duda, G. N. (1995). "The course of bone healing is influenced by the initial shear fixation stability." *Journal of Orthopaedic Research*, 9, 324-332.
- Claes, L. (2011). "Biomechanical principles and mechanobiologic aspects of flexible and locked plating." *Journal of orthopaedic trauma*, 25 Suppl 1, S4-7.
- Claes, L., Reusch, M., Göckelmann, M., Ohnmacht, M., Wehner, T., Amling, M., Beil, F. T., and Ignatius, A. (2011). "Metaphyseal fracture healing follows similar biomechanical rules as diaphyseal healing." *Journal of Orthopaedic Research*, 29(3), 425-432.
- Döbele, S., Horn, C., Eichhorn, S., Buchholtz, A., Lenich, A., Burgkart, R., Nüssler, A. K., Lucke, M., Andermatt, D., Koch, R., and Stöckle, U. (2010). "The dynamic locking screw (DLS) can increase interfragmentary motion on the near cortex of locked plating constructs by reducing the axial stiffness." *Langenbeck's archives of surgery / Deutsche Gesellschaft für Chirurgie*, 395, 421-8.
- Doornink, J., Fitzpatrick, D. C., Madey, S. M., and Bottlang, M. (2011). "Far cortical locking enables flexible fixation with periarticular locking plates." *Journal of orthopaedic trauma*, 25 Suppl 1, S29-34.
- Epari, D. R., Taylor, W. R., Heller, M. O., and Duda, G. N. (2006). "Mechanical conditions in the initial phase of bone healing." *Clinical biomechanics (Bristol, Avon)*, 21, 646-55.
- Gardner, M. J., Nork, S. E., Huber, P., and Krieg, J. C. (2009). "Stiffness modulation of locking plate constructs using near cortical slotted holes: a preliminary study." *Journal of orthopaedic trauma*, 23, 281-7.
- Gardner, M. J., Nork, S. E., Huber, P., and Krieg, J. C. (2010). "Less rigid stable fracture fixation in osteoporotic bone using locked plates with near cortical slots." *Injury*, 41, 652-6.
- González-Torres, L. A., Gómez-Benito, M. J., Doblaré, M., and García-Aznar, J. M. (2010). "Influence of the frequency of the external mechanical stimulus on bone healing: A computational study." *Medical Engineering & Physics*, 32, 363-371.
- Goodship, A. E. (1985). "The influence of induced micromovement upon the healing of experimental tibial fractures." *Journal of Bone and Joint Surgery*, 67(4), 650.
- Hak, D. J., Toker, S., Yi, C., and Toreson, J. (2010). "The influence of fracture fixation biomechanics on fracture healing." *Orthopedics*, 33, 752-5.
- Henderson, C. E., Bottlang, M., Marsh, J. L., Fitzpatrick, D. C., and Madey, S. M. (2008). "Does locked plating of periprosthetic supracondylar femur fractures promote bone healing by callus formation? Two cases with opposite outcomes." *The Iowa orthopaedic journal*, 28, 73-6.
- JH, K., and SH, C. (2007). "Design of a flexible composite bone plate for bone fracture healing." 14th international conference on composite structures, Melbourne, Australia.
- Kim, S.-H., Chang, S.-H., and Jung, H.-J. (2010). "The finite element analysis of a fractured tibia applied by composite bone plates considering contact conditions and time-varying properties of curing tissues." *Composite Structures*, 92, 2109-2118.
- Klein, P. (2003). "The initial phase of fracture healing is specifically sensitive to mechanical conditions." *Journal of Orthopaedic Research*, 21(4), 662.
- Klein, P., Schell, H., Streitparth, F., Heller, M., Kassi, J.-P., Kandziora, F., Bragulla, H., Haas, N. P., and Duda, G. N. (2003). "The initial phase of fracture healing is specifically sensitive to mechanical conditions." *Journal of Orthopaedic Research*, 21, 662-669.
- Lacroix, D., and Prendergast, P. J. (2002). "A mechano-regulation model for tissue differentiation during fracture healing: analysis of gap size and loading." *Journal of Biomechanics*, 35, 1163-1171.
- Lujan, T. J., Henderson, C. E., Madey, S. M., Fitzpatrick, D. C., Marsh, J. L., and Bottlang, M. (2010a). "Locked plating of distal femur fractures leads to inconsistent and asymmetric callus formation." *Journal of Orthopaedic Trauma*, 24(3), 156-162.

- Lujan, T. J., Henderson, C. E., Madey, S. M., Fitzpatrick, D. C., Marsh, J. L., and Bottlang, M. (2010b). "Locked plating of distal femur fractures leads to inconsistent and asymmetric callus formation." *Journal of orthopaedic trauma*, 24, 156-62.
- Mccartney, W., Donald, B., and Hashmi, M. (2005). "Comparative performance of a flexible fixation implant to a rigid implant in static and repetitive incremental loading." *Journal of Materials Processing Technology*, 169, 476-484.
- Miller, D. L., and Goswami, T. (2007). "A review of locking compression plate biomechanics and their advantages as internal fixators in fracture healing." *Clinical biomechanics (Bristol, Avon)*, 22, 1049-62.
- Oloyede, A., and Broom, N. D. (1991). "Is classical consolidation theory applicable to articular cartilage deformation?" *Clinical Biomechanics*, 6(4), 206-212.
- Oloyede, A., and Broom, N. D. (1994). "The generalized consolidation of articular cartilage: an investigation of its near-physiological response to static load." *Connective Tissue Research*, 31(1), 75-86.
- Perren, S. M. (2002a). "Evolution of the internal fixation of long bone fractures. The scientific basis of biological internal fixation: choosing a new balance between stability and biology." *The Journal of Bone and Joint Surgery*, 1093-1110.
- Perren, S. M. (2002b). "Evolution of the internal fixation of long bone fractures: the scientific basis of biological internal fixation: choosing a new balance between stability and biology." *Journal of Bone and Joint Surgery*, British Volume, 1093-1110.
- Plecko, M., Lagerpusch, N., Andermatt, D., Frigg, R., Koch, R., Sidler, M., Kronen, P., Klein, K., Nuss, K., Bürki, A., Ferguson, S. J., Stoeckle, U., Auer, J. a., and von Rechenberg, B. (2012). "The dynamisation of locking plate osteosynthesis by means of dynamic locking screws (DLS)-An experimental study in sheep." *Injury*.
- Prendergast, P. J., Checa, S., and Lacroix, D. (2010). "Computational models of tissue differentiation " *Computational Modeling in Biomechanics*, 3, 353-372.
- Rabiei, A. (2010). "Recent developments and the future of bone mimicking: materials for use in biomedical implants." *Expert review of medical devices*, 7, 727-9.
- Rabiei, A. (2012). "Composite metal foam and methods of preparation thereof."
- Sellei, R. M., Garrison, R. L., Kobbe, P., Lichte, P., Knobe, M., and Pape, H.-C. (2011). "Effects of near cortical slotted holes in locking plate constructs." *Journal of orthopaedic trauma*, 25 Suppl 1, S35-40.
- Stoffel, K., Dieter, U., Stachowiak, G., Gächter, A., and Kuster, M. S. (2003). "Biomechanical testing of the LCP – how can stability in locked internal fixators be controlled?" *Injury*, 34, 11-19.
- Szypryt, P., and Forward, D. (2009). "The use and abuse of locking plates." *Orthopaedics and Trauma*, 23(4), 281-290.
- Thompson, Z., Miclau, T., Hu, D., and Helms, J. a. (2002). "A model for intramembranous ossification during fracture healing." *Journal of orthopaedic research : official publication of the Orthopaedic Research Society*, 20, 1091-8.
- Zdero, R., and Bougherara, H. (2010). "x Orthopaedic Biomechanics : A Practical Approach to Combining Mechanical Testing and Finite Element Analysis." 171-194.
- Zhang, L., Gardiner, B. S., Smith, D. W., Pivonka, P., and Grodzinsky, A. J. (2007). "The effect of cyclic deformation and solute binding on solute transport in cartilage." *Archives of Biochemistry and Biophysics*, 457(1), 47-56.
- Zhang, L., Gardiner, B. S., Smith, D. W., Pivonka, P., and Grodzinsky, A. J. (2008). "A fully coupled poroelastic reactive-transport model of cartilage." *Molecular & Cellular Biomechanics*, 5(2), 133-153.
- Zhang, L., Gardiner, B. S., Smith, D. W., Pivonka, P., and Grodzinsky, A. J. (2009). "Integrated model of IGF-I mediated biosynthesis in deforming articular cartilage." *Journal of Engineering Mechanics (ASCE)*, 135(3), 439-449.
- Zhang, L., Richardson, M., and Mendis, P. (2012). "Role of chemical and mechanical stimuli in mediating bone fracture healing." *Clinical and Experimental Pharmacology and Physiology*, 39, 706-710.