In Silico Fracture Healing using Fuzzy Logic: Union and Nonunion

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Summary

The fracture healing process entails a host of biological processes and signaling. In this study, an *in silico* model was developed to capture these in a phenomenological way, with an emphasis on the effects of mechanical loading. The presence of five tissues (granulation tissue, fibrous tissue, soft cartilage, mineralized cartilage and woven bone), along with the perfusion of blood, is computed over time with a fuzzy logic controller which, in addition to the existing tissue concentrations, makes use of dilatational and distortional strains extracted from a structural finite element analysis. The model is able to correctly predict (non)union under various amounts of mechanical stability.

Introduction

The most common type of fracture healing is secondary or indirect bone healing. In this type of healing, both intramembranous and endochondral ossification take place. The latter form of ossification is preceded by chondrogenesis and the mineralization of the formed cartilage matrix. Oxygen and nutrients are transported through the blood and reach specific areas of the fracture callus by the growth of new blood vessels (angiogenesis). The perfusion of blood is a key factor that allows both intramembranous and endochondral ossification to take place.

Fuzzy logic (computational) models of fracture healing have been developed since 2000 by Ament and Hofer [1], and a significant contribution was made by Simon et al. [2], incorporating the perfusion of blood into these models. However, two simplifications, being the utilization of 'connective tissue' to refer to both granulation and fibrous tissue, and the incorporation of cartilage mineralization directly into the woven bone state variable, are a limit to its biological accuracy and inhibit this model from being able to predict nonunion. In this study, a new model is proposed, taking into account the aforementioned distinction and the addition of the mineralized variant of cartilage.

Materials and methods

In this computational model using fuzzy logic, a set of rules determines the presence of five tissues: granulation tissue, fibrous tissue, soft cartilage, mineralized cartilage and woven bone, along with the perfusion of blood. These rules describe angiogenesis, intramembranous ossification, fibrous tissue formation, chondrogenesis, cartilage mineralization, endochondral ossification and atrophy. In order to capture the mechanical loading of the tissues, a finite element analysis is performed and distortional and dilatational strains are extracted. To correctly model angiogenesis, ossification and cartilage mineralization, adjacent values of perfusion and woven bone concentration are regarded as well. The growth over time is captured by the iterative calculation of all input variables ($c_{perfusion}$, $c_{perfusion,\ adj.}$, $c_{fibr.\ tiss.}$, $c_{soft\ cart.}$, $c_{min.\ cart.}$, $c_{wov.\ bone}$, $c_{wov.\ bone,\ adj.}$, $\varepsilon_{dist.}$ and $\varepsilon_{dila.}$) and output variables ($\Delta_{perfusion}$, $\Delta_{fibr.\ tiss.}$, $\Delta_{soft\ cart.}$, $\Delta_{min.\ cart.}$ and $\Delta_{wov.\ bone}$).

The healing of an ovine metatarsus osteotomy [3] was simulated under normal loading (500 N of sheep body weight in axial direction) with four different external fixators: overly stiff, reasonably stiff, reasonably flexible and overly flexible.

Results and Discussion

Fig. 1 shows the results of the simulation when a steady state has been reached. With a reasonably flexible or stiff fixator, an appropriately sized bony callus has developed, ready for remodeling. With the stiffer fixator, the callus forms faster, but less abundant. With an overly stiff fixator, the callus is underdeveloped and prone to refracture, but a bony bridge is formed. Contrarily, with overly flexible fixation, a stroke of fibrous tissue and soft cartilage remains.

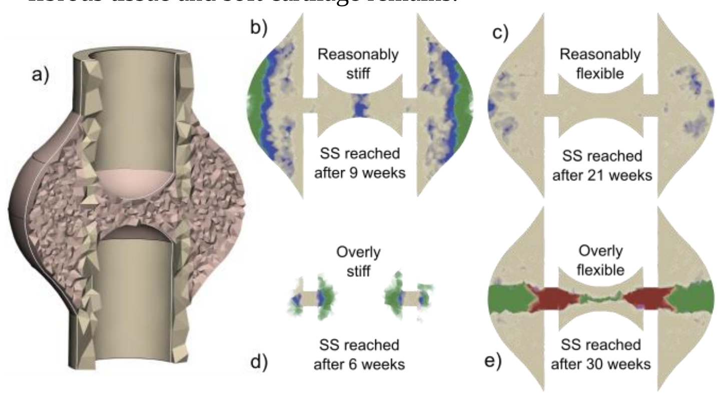

Figure 1: Bone and callus geometry (a) and presence of tissues at steady state (SS) (b, c, d, e). (red = fibrous tissue, green = soft cartilage, blue = mineralized cartilage, beige = woven bone)

Conclusions

The developed fracture healing model is able to distinguish between union and nonunion by capturing the biological processes in a phenomenological way.

Acknowledgements

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References

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