A MESHLESS LOCAL BOUNDARY INTEGRAL EQUATION (LBIE) METHOD FOR PREDICTION OF CELL NON-LINEAR DIFFUSION DURING BONE HEALING

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Introduction

Bone fracture healing is a complex regenerative process that includes cellular events that have not yet been elucidated. Most of the computational models examining the effect of mechanical stimuli on biological pathways during healing describe cellular mechanisms via diffusion equations commonly solved using the Finite Element Method (FEM). Although FEM is robust it suffers from global remeshing when new born surfaces or material phases appear in the problem. This is encountered by using meshless methods in which no background cells are needed for the numerical solution of the integrals [Sellountos, 2008]. In this study a new meshless Local Boundary Integral Equation (LBIE) method is employed for solving non-linear the diffusion equation that describes cell proliferation and derives predictions of cell distribution during bone healing.

Methods

We considered the concentration of all cell types to satisfy the diffusion equation

$$\partial_t c(\mathbf{x},t) = D\nabla^2 c(\mathbf{x},t) + f_{pr} c^2(\mathbf{x},t) - F_{dif} - F_{ap}$$

where ∂_t indicates differentiation with respect to time, $\mathbf{x}$ is the position vector of a point in a two dimensional space, ∇ represents the gradient operator, D is the diffusivity of the cells, and f_{pr}, F_{dif}, F_{ap} parameters that regulate rates of proliferation, apoptosis and differentiation, respectively. The geometrical model of the callus tissue was based on previous 2D mechanical model of healing bone. The inner and outer diameters were 14 mm and 20 mm. Cell parameters were considered equal to those of mesenchymal stem cells (MSC). The initial conditions in the model included concentrations of MSC at the periosteum, the marrow interface and the interface between bone and callus at the fracture site. Flux across the remainder external boundaries was also constrained. Numerical calculations were performed for 25 days post-fracture.

Results

The mesenchymal cells proliferation was found to start in the fracture gap. Increased MSC concentrations were also found along the periosteum at some distance from the gap. MSCs were also found to proliferate in the periosteum but closer to the fracture site. A significant increase of cell concentrations was also found in the fracture gap at the last days which suggests that progressive intramembraneous ossification occurs possibly followed by endochondral replacement.

Discussion

A new meshless LBIE method was implemented for deriving predictions about MSC concentration during bone healing. Cell diffusion was described by non-linear equation. Numerical simulations were performed in a 2D computational model. Overall meshless LBIE method could capture significant events that occur during bone healing and could be thus considered as a significant tool for solving diffusion problems.

References

[1] E. J Sellountos et al., CMES, 41: 474-483 2008.