Tissue Differentiation Steps Towards Bone Formation

PJ Prendergast[1] DP Byrne[1], DJ Kelly[1], D Lacroix[2]

[1]*Trinity Centre for Bioengineering, School of Engineering, Trinity College, Dublin, Ireland,*
[2]*Institute of Bioengineering of Catalonia, Department of Metallurgy and Materials Engineering, Technical University of Catalonia, Barcelona, Spain*

INTRODUCTION: When an implant is inserted into the body it immediately changes the stress and strain distribution in the tissues in its immediate environment. This is particularly relevant for load-bearing orthopaedic implants, but it is also critical for tissue-engineered constructs (implants) as they are required to elicit a proliferation and differentiation response from the cells that are either seeded within them *in vitro*, or migrate into them on implantation. To design these implants methods to predict the response of tissues to the changing mechanical environment are required [1]. Here we describe an approach to predicting how the scaffold design parameters may determine the degree of bone formation of Calcium Phosphate (CaP) bioceramics used as a scaffold in bone tissue engineering.

MATERIALS & METHODS: Taking the parameter *S*, as defined below, as a stimulus governing tissue differentiation:

$$S = \frac{\gamma}{a} + \frac{v}{b} \tag{1}$$

where γ is the shear strain and v is the relative fluid/solid velocity; both of these stimuli will distort progenitor cell shape and the hypothesis is that the value of this stimulus will determine the propensity to form bone, cartilage, or fibrous connective tissue[2]. To simulate bone regeneration in a scaffold, we use *S* together with the following features to create a mechano-regulation algorithm: [i] discretize the domain into 'lattice points' with such points being either empty, or containing a precursor or differentiated cell, [ii] simulate proliferation by mitosis to occupy vacant neighboring lattice points, [iii] use a random-walk model to simulate cell migration, [iv] use an exponential function to simulate growth in matrix around a cell. These features are combined with an FEM of a regular CaP scaffold. Table 1 shows the design parameters analysed.

Porosity (%)	30	50	70
Modulus (MPa)	750	1000	1250
Dissolution rate (%/iter.)	0	0.5	1

Table 1: Matrix of design parameters simulated for the scaffold

RESULTS AND DISCUSSION: It was predicted that the design parameters had a critical effect on the amount of bone regeneration, but not in an obvious way (see Fig.1). For example, if the dissolution rate is high then high Young's modulus is best; however this is true only for the high or low porosity (Fig. 1)

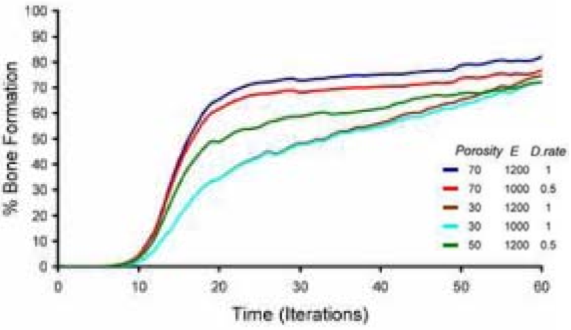

Figure 1: A plot of the increase in the amount of bone in the scaffold for various combinations of porosity, dissolution rate, and Young's modulus (at a load of 1 MPa applied to a 7 mm^3 scaffold).

Figure 1 shows results under a relatively low load regime; if the load is higher predictions show that a low porosity and high dissolution rate is a bad combination because the scaffold can collapse. In general we can conclude that a scaffold should be optimally designed to allow" steps to bone formation". Indeed it might be that scaffolds should be designed for specific skeletal sites depending on the loads or displacements acting there.[3]

REFERENCES: [1] D.J. Kelly, P.J. Prendergast, *Tissue Eng*. (2006) **12**, 2509-2519. [2] D. Lacroix, P.J. Prendergast (2002) *J. Biomech.* **35**, 1163-1171. [3] Prendergast *et al. J. Biomech*.(1997) **30**, 539-548

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