Simple Optimization of Gradated Biomaterial Scaffolds made of Calcium Phospates

One of the mainstreams of modern biomaterials is the application of calcium hydroxyapatite (HAP) [1,2]. Various combinations of HAP as scaffolds and coatings or as a component of bioceramics and composites are being tested. To enhance osteoconductivity and osteointegraton, additions of other calcium phosphates (*CP*) like beta-tricalcium phosphate $Ca_3(PO_4)_2$ *(ß-TCP)*, glass-ceramics etc. are being exploited. Different processing methods of these compounds result in a variety of their mechanical, chemical and biological properties, which is also affected by density (porosity) and possible cross-interactions. There are also differences between in vitro and in vivo conditions, and not all of them are precisely known.

Earlier homogeneous compositions of *HAP+(25…75%) ß-TCP* have been considered as the compromise solution for optimal osteointegration, since *ß-TCP* is known to dissolve faster in both simulated body fluid (SBF) and in vivo conditions [2], although this also depends on porosity and crystal size. Protein adsorption on HAP delays bone formation, so a compromise solution should be sought to balance all these factors to ensure proper osteointegration.

It has been suggested that a functionally gradated material (FGM) with a smoothly changing concentration and porosity profile would provide a better solution for the implants and scaffolds [2]. This kind of controlled porous material can be manufactured by a powder metallurgy technique with mixing and sintering. The latter however leads to generation of thermal stresses due to the difference in thermal expansion and sintering rates. Thus in the case of a FGM disk, this will lead to bending and twisting, up to possible cracking. Uneven stresses and remained porosity will not guarantee proper bioresorbabilty of the material - degradation of CP occurs preferentially on grain boundaries when the soluble phases disappear and the grains of less-soluble CP phases are released into a body environment. Such particle release is a cause of concern due to osteolysis (bone loss).

To define the most optimal FGM profile including thermal and sintering residual stresses over the whole processing range, kinetics of co-sintering of HAP and *ß-TCP* should be analysed and the experimental data fed into the sintering model. The developed generic model of sintering [3,4] is based on visco-elasto-plastic behaviour of the material, when its properties depend on porosity and grain size, coupled with thermal expansion. For example, for pure HAP it was experimentally found that the sintering kinetics could be approximated (±10% error) with Avraami-Erofeev's equation:

$$\frac{d\alpha}{d\tau} = -A(\rho_0)\exp\left(-\frac{E}{RT}\right)\cdot n(\rho_0)\cdot\alpha\cdot\left[-\ln(\alpha)\right]^{\frac{n(\rho_0)-1}{n(\rho_0)}}$$

where α – degree of sintering as measured by dilatometry. Explicit solution of this differential equation for shrinkage is:

$$\alpha(T,\tau) = \exp\left[-\left(\frac{A(\rho_0)\int_0^{\tau}\exp\left(-\frac{E}{RT}\right)d\tau}{n(\rho_0)}\right)^{n(\rho_0)}\right],$$

for any programmable heating rate. When sintering a mixture, the shrinkage is more complex and a numerical fitting is usually required to incorporate it into models [3,4]. Fig. 1 shows the measured and interpolated shrinkage of *HAP + ß-TCP* mixtures. It could be seen that with <20% of *HAP* in the mixture, shrinkage remains low until high temperatures, and for mixtures with >60% *HAP,* it does not deviate too much from the pure HAP.

Using experimental data and equations for thermal expansion and contraction, the MathCAD model for thermal stresses of FGM with arbitrary thickness and gradation profile has been set up. Properties of FGM were calculated using a

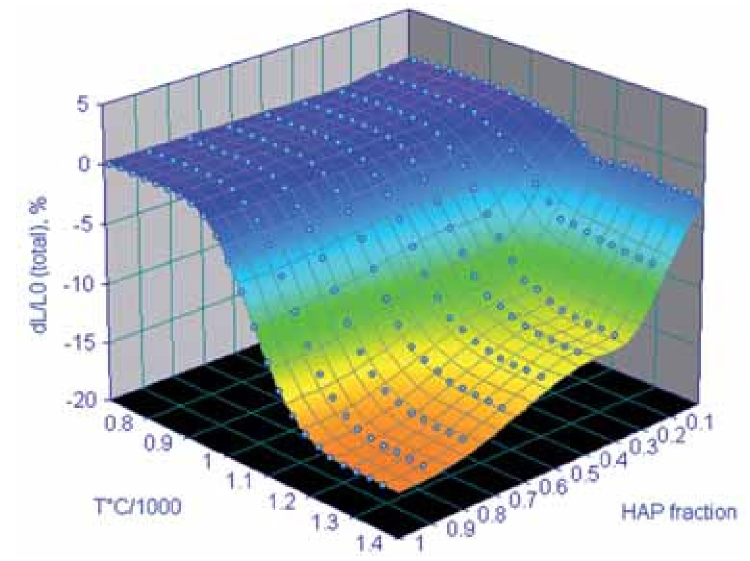

Fig. 1 - Interpolated global shrinkage of the HAP + ß-TCP composites from 700°C.

micromechanical model [4] and the simplified stress analysis was preformed using the linear plate theory. The gradation profile was assumed to follow a power function:

$$V_{HAP} = \left(\frac{x}{H_{FGM}} \right)^{P},$$

where the volume fraction of HAP depends on x (the thickness coordinate), H_{FGM} (thickness of the FGM layer (1…5 mm)) and P – gradation parameter (0.01… 100).

Because stress evolution is non-linear for processing temperature and composition, it is necessary to establish single integral variables, which represent some measure of these stresses and relate them to other compositions with different thickness and gradation. Global integrated parameters chosen for this analysis are stress derivatives differences (S_1), combined averaged stress difference (S_2) and combined curvature of the FGM plate (S_3):

$$S_1 = \frac{1}{T_{\sin} - T_0} \int_{T_0}^{T_{\sin}} \sqrt{\frac{1}{H} \sum_x \left(\frac{d\sigma(x,T)}{\partial x} - \frac{1}{H} \sum_x \left| \frac{\partial \sigma(x,T)}{\partial x} \right| \right)^2} \, dT$$

$$S_2 = \frac{1}{T_{\sin} - T_0} \int_{T_0}^{T_{\sin}} \sqrt{\frac{1}{H} \sum_x \left(\sigma(x,T) - \frac{1}{H} \sum_x \left| \sigma(x,T) \right| \right)^2} \, dT$$

$$S_3 = \frac{1}{T_{\sin} - T_0} \int_{T_0}^{T_{\sin}} C_1(T) \, dT$$

The choice of these parameters instead of traditional ones was dictated by the need of a single parameter, which is capable of integration of information about the whole FGM plate during the whole temperature range from beginning of sintering (T_0) to sintering temperature (T_{sin}), without explicit analysis of stresses in every point at every time and temperature step. It is known from FGM barrier coatings optimization that stress differences and their derivative differences are also important for material performance besides the absolute stress magnitude. The criteria S_1 and S_2 do not distinguish between tensile and compressive stresses but consider only their absolute values and thus might be overcautious in indication of "optimal" gradation. Nevertheless, they are believed to represent the general trends and to define the area, which would be further analysed using numerical methods in more detail. The objective of finding this optimal gradation is in minimising of all three criteria S_1-S_3.

The model was set up with modeFRONTIER® 4.1.2, using a single MathCAD node for model calculation. Stored results were exported to Grapheur 1.0 visualisation software, where these stress differential changes (S_1), averaged stress difference (S_2) and averaged curvature (S_3) were analysed as functions of the input variables gradation parameter P (and log(P)) and thickness H_{FGM}.

It is expected that thicker layer will have much less curvature. FGM with a large value of P seems to have the least stress difference for all thicknesses analysed. When all three S-criteria are plotted together (Fig. 2), the effect of gradation parameter (colour) is clearly more important than the thickness. Whereas mean values of P (green bubbles), corresponding to near linear gradation, provide minimum of S_1, this does not automatically guarantee minimum of S_2 values neither curvature (S_3).

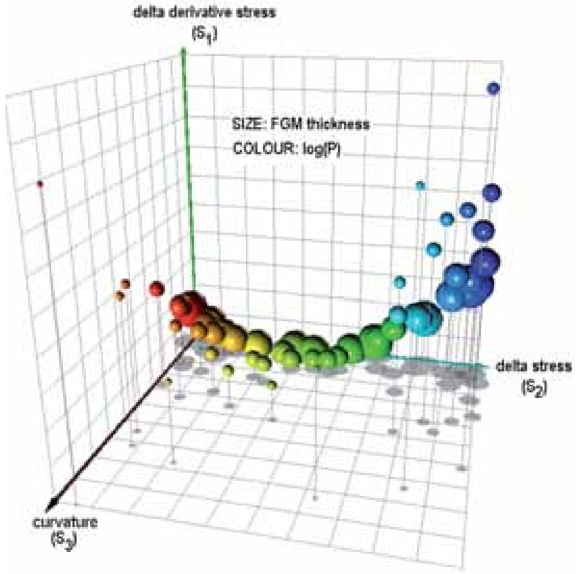

Fig. 2 - Mutual dependence of all criteria. The best solutions are located closest to the coordinates origin.

Fig. 2 shows that that thicker FGM plates (larger bubbles) with a larger gradation parameter (red colour), i.e. a thin graded layer (~20% of the total thickness of the β-TCP layer) will lead to the lowest curvature, stresses and their derivatives during the whole sintering process. In the case of the optimised profile, this HAP-rich layer with lower porosity and dissolution rate might provide an interesting effect on osteointegration as well. This is expected to ensure better stability of the scaffold in the body after implantation due to less destructive acting of internal stresses. In the future, more complicated geometries and different sintering regimes might be also simulated to find out the optimal set of processing parameters.

References

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