

Influence of pore geometry on vascular colonization of porous silicon-substituted hydroxyapatite ceramics shaped by microstereolithography

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Owing to its chemical composition close to that of the mineral bone, hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) is a osteoconductive material commonly used in bone surgery. While controversial, silicon substitution for phosphorus in the HA lattice was described to enhance its biological properties. Beyond the effects due to the size and the architecture of scaffolds, cell colonisation of biomaterials is influenced by numerous parameters including pore geometry. Theoretical models have been established to relate tissue growth with the pore shape, main geometrical parameters of influence being the radius of curvature, the convexity and the presence and size of angles.

In the present work, the influence of pore geometry on vascularization of microstereolithographed SiHA ceramics was quantitatively evaluated in an expedient adaptation of the *ex ovo* model of the chick embryo chorio-allantoic membrane (CAM).

SiHA ceramics with pores of different geometries (circular, square, triangles, rhomboids star-like cross-section) were implanted on the CAM model. Resulting images of the vascularized implants were analyzed considering specific parameters (vascular density, hierarchisation, number and blood vessel diameter, fractal dimensions...) on two-scales (whole implant scale and pores).

Implantation of ceramics did not affect embryos and the well-adhering CAM tissue in which they were embedded that confirmed their total biocompatibility. The implants were well vascularized, blood vessels appeared to be guided towards pores.

Whole implant image analyses revealed a higher vascular density on unporous ceramics due to the large diameter of first generation of blood vessels. Other parameters relative to the angiogenesis were not affected by the presence of pores (fractal dimensions, number of branching points...).

Focusing the analysis to the pore-converging blood vessels revealed that their number increased for rhomboid and triangular pores in comparison with circular ones. Moreover their average diameter was higher for triangular pores being consequently the more attractive shape. This effect was attributed to the sharpness of angles that is consistent with theoretical models elaborated on pore angle colonization by cells (curvature-driving force models and derivatives).

Here we show that the pore geometry influences the biological properties of stereolithographed SiHA ceramics concerning their vascular colonization (namely angiogenic properties) on the CAM model. Especially was highlighted the pro-angiogenic effect of sharp angles (triangular pores) when compared to pores with no (circular) or larger angles (rhomboid). Based on these results, 3D scaffolds with such pores were produced and implanted in rats for advanced investigations.