What is the optimum pore structure for osteoconductivity and osteoinductivity of porous bioactive titanium?

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Introduction: Osteoconductivity is generally interpreted to mean the apparent growth of bone tissue ‘along’ an implant’s surface. Osteoconductive materials include processed human bone (‘allograft bone’), purified collagen, Bioglass, several calcium phosphate ceramics, glass ceramic A-W, and chemically and thermally treated porous titanium (1). Osteoinduction, as opposed to osteoconductivity, is a biological process that induces local mesenchymal cells to differentiate into bone-producing cells. When some osteoconductive biomaterials have a specific porous structure, they are known to become osteoinductive in soft tissues without the addition of osteogenic cells or BMPs. (2, 3) Osteoconductivity and osteoinduction are now recognized as being important for stable long-term implant fixation. There are three important features of the osteoconductivity and osteoinductivity of the biomaterials: surface chemistry, surface topography, and architectural geometry (porous structure). In this study, we investigate the effect of macroporous structure on the osteoconductivity and osteoinductivity of porous bioactive titanium implants. Macroporous structure was evaluated using mercury porosimetry and micro-CT data. Osteoconductivity was evaluated using a rabbit femoral condyle bone model and osteoinductivity was evaluated by implantation into the back muscles of adult beagle dogs.

Materials and Methods: Implants: Four types of sintered porous titanium implants with different porosities and pore sizes (ST50–250 (target porosity = 50%, spacer particle size used = 250–500 μm), ST50–500 (50%, 500–1500 μm), ST70–250 (70%, 250–500 μm), and ST70–500 (70%, 500–1500 μm)) were manufactured by controlling the amount and size of the spacer particles, as previously described. (Figure 1)(4) Cylinders 6 mm in diameter and 15 mm long were cut from a porous layer using electric-discharge machining. These cylinders were treated chemically and thermally as previously described. (3) Titanium implants were supplied by Osaka Yakin Co. (Osaka, Japan).

Micro-CT analysis: The pore structure of the porous titanium was examined using a micro-CT system (SMX-100CT-SV3; Shimadzu, Japan) as previously described. (4)

Mercury porosimetry: Using a mercury intrusion porosimetry (AutoPore IV 9500, Shimadzu, Kyoto, Japan), the pore size distribution of each implant was expressed as cumulative pore volume percent (the cumulative pore volume per total pore volume) as a function of pore diameter.

Animal experiments: This animal study was approved by the Animal Research Committee, Graduate School of Medicine, Kyoto University, Japan. For analysis of osteoconductivity, four types of implants were implanted in the dorsal muscles of four mature beagle dogs for periods of three and six months. For analysis of osteoconductivity, implants were implanted in the femoral condyle of adult male Japanese white rabbits for six and 12 weeks. At six and 12 weeks after implantation, four rabbits were killed using an overdose of intravenous pentobarbital sodium, that is, four implants and four animals were used per experimental condition. Each implant was examined histologically and new bone area rates were calculated from measurements of each implant.

Results: Analysis of the Pore Structures: Both micro-CT and mercury porosity analysis revealed that over 99% of pores were connected to the outside in all implants. In ST70s (porosity of 70%), most pore throats (> 80%) had a diameter of more than 75 μm. However, in ST50s, only 30% of pore throats had a diameter of more than 75 μm.

Results of the animal experiments: In orthotopic implantation at six weeks, more bone with marrow tissue was observed in ST70s and osteoconductivity was superior in these groups. In contrast, as for osteoinduction, ST50s showed superior bone forming ability in dog muscles at three and six months compared with ST70s.

Discussion: The results of the current study indicate that an interconnected concave pore structure with a relatively narrow pore throat seems to be optimum for an osteoinductive biomaterial. The protected pore area with isolated environment without strong fluid movement may be favorable for osteoinduction. In contrast, as previously reported, these narrow pore throats were not suitable for bone ingrowth in orthotopical implantation. (4) Regarding the surface characteristics (chemistry and topography) of biomaterials, the optimum conditions for the improved osteoinductivity appear to parallel those required for higher osteoconductivity (3); however, porous structure may have a more complex influence on the biological response to biomaterials.