Nano-technological Control of Biomaterial-Hard Tissue Interfaces

Yasuhiro Yoshida[1), 2)], Bart Van Meerbeek[3)], Yoshihiro Ito[4), 5)], Kazuomi Suzuki[1), 2)]

[1)] *Department of Biomaterials, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science, Okayama, Japan*
[2)] *Research Center for Biomedical Engineering, Okayama University, Okayama, Japan*
[3)] *Leuven BIOMAT Research Cluster, Department of Conservative Dentistry, School of Dentistry, Oral Pathology and Maxillo-Facial Surgery, Catholic University of Leuven, Leuven, Belgium*
[4)] *Regenerative Medical Bioreactor Project, Kanagawa Academy of Science and Technology, Kanagawa, Japan*
[5)] *Nano Medical Engineering Laboratory, RIKEN (The Institute of Physical and Chemical Research), Saitama, Japan*

Abstract：Adhesives for tooth bonding, implants, bone substitutes, bone cements, etc. are widely used for functional reconstruction of human hard tissues, such as bone and tooth tissue. The success of these treatments depends to a large extent on the properties of the resultant biomaterial-hard tissue interface. Thus, it is our belief that if the biomaterial surface can be nano-technologically controlled, more intense interaction of the biomaterial with the hard tissue can be achieved. In this paper, we report on three examples of nano-technological control of biomaterial-hard tissue interfaces, as there are the bonding of a so-called dental self-etch adhesive to tooth tissue, the integration of biological apatite in bone and the modification of the surface of Ti implants to promote cell attachment and growth.

Keywords: tooth bonding, apatite, Ti implant.

Introduction

Dental therapy often consists of functional reconstruction of human hard tissues, such as bone and tooth tissues. Decayed or traumatized teeth can be restored by bonding the biomaterial directly to the remaining sound tooth tissue. In case a tooth is missing, an implant can be inserted in the bone of the jaw as a support for a crown. Bone resorption in jaws can be treated with bone-substitute materials that fully integrate in the remaining bone tissue. Although these three therapies are completely different and totally different biomaterials are employed to reconstruct the hard tissue, the longevity of these reconstructions strongly depends on the properties of the resultant interface between the biomaterial and the hard tissue. Thus, if the biomaterial-hard tissue interface can be nano-technologically controlled, the interaction of the biomaterial with the hard tissue can be improved with direct benefit to the longevity of the hard-tissue reconstruction.

The aim of this paper is to present three examples of nano-technological control of biomaterial-hard tissue interfaces. (1) As the main component of dental adhesives is the functional monomer, we will show how the molecular structure of the functional monomer determines how intense and stable the biomaterial interacts with enamel and dentin; (2) we will demonstrate how functionally graded $MgCO_3$apatite can be very effective as bone-substitute material; and (3) how the surface of Ti implants can be modified with photo-reactive gelatin in order to promote selective cell attachment and growth.

Tooth bonding

Bonding to tooth tissue, especially to dentin, is based primarily on micro-mechanical interlocking by a process known as the formation of a hybrid layer or hybridization. The longevity of adhesive tooth restorations depends to a large extent on the quality of the hybrid layer. Among dental adhesives, so-called 'mild' self-etch adhesives only partially demineralize dentin, and leave apatite around collagen within a submicron hybrid layer. This residual apatite serves as receptor for chemical interaction with the functional monomer of the adhesive. This chemical interaction, in addition to the process of micro-mechanical hybridization, is especially thought to contribute to the stability of the adhesive-tooth bond. We therefore characterized the chemical interaction of three representative functional monomers with synthetic hydroxyapatite using X-ray Photoelectron Spectroscopy and Atomic Absorption Spectrophotometry. The monomer 10-methacryloxydecyl dihydrogen phosphate (10-MDP) was shown to readily adhere to hydroxyapatite. Moreover, its bond appeared very stable, as was confirmed by the low dissolution rate of its calcium salt in water. The bonding potential of 4-methacryloxyethyl trimellitic acid (4-MET) was substantially lower. The monomer 2-methacryloxyethyl phenyl hydrogen phosphate (phenyl-P) and its bond to hydroxyapatite appeared not very hydrolytically stable[1)]. These chemical data closely correspond to micro-tensile bond strength (method to determine the strength of the bond) data. The micro-tensile bond strength of the 10-MDP-based adhesive did not decrease significantly after 100,000 thermo-cycles (a procedure used to challenge the biomaterial-hard tissue interface), it did after 50,000 and 30,000 cycles, respectively, for the 4-MET-based and the phenyl-P-based adhesive[2)]. Likewise, the interfacial ultra-structure (as observed ultra-morphologically using TEM) remained unchanged after 100,000 thermo-cycles for the 10-MDP-based adhesive, while that of both the 4-MET- and phenyl-P-based adhesives contained voids and less defined collagen[2)]. The findings of this study support the concept that the chemical bonding potential of the functional monomer contributes to the long-term durability of adhesive-dentin bonds.

Functionally graded CO_3-apatites as bone-substitute materials

Correspondence to Yasuhiro Yoshida, Department of Biomaterials, Okayama University Graduate School of Medicine and Dentistry, 2-5-1 Shikata-cho, Okayama 700-8525, Japan. TEL: +81-86-235-6666, FAX: +81-86-235-6669. E-mail: yasuhiro@md.okayama-u.ac.jp

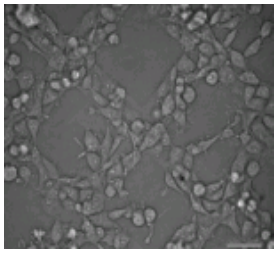

Fig. 1. Micro-pattern formation of COS-7 cells attached to immobilized gelatin regions on the Ti surface. Bar = 50μm.

Apatite, which is the main component of hard tissues such as bone and teeth, contains many trace elements. To improve the biological properties of bone substitute materials, functionally graded CO_3 apatite crystals that contain magnesium, referred to as $FGMgCO_3Ap$, were synthesized at 60°C and at a pH of 7.4 using a gradient magnesium supply system[3]. Next, they were mixed with collagen in order to fabricate a composite pellet with a crystallinity close to that of bone. A radio-labeled cell adhesion experiment showed that the degree of adherence of mouse MC3T3E1 osteoblast-like cells to the $FGMgCO_3Ap$-collagen composite was better than to CO_3Ap-collagen composite and much better than to pure Ti[4]. When in a next experiment such $FGMgCO_3Ap$-collagen composites were implanted into the femur of rabbits, clear bone formation with a higher degree of bone density was observed[4]. These results suggest that the Mg^{2+} ions absorpted within the apatite crystals may accelerate the adhesion of osteoblasts to the apatites and thus promote bone formation.

Surface modification of Ti implants

The titanium surface was modified with photo-reactive gelatin in order to regulate cell attachment. Photo-reactive gelatin was synthesized by coupling gelatin with *N*-(4-azidobenzoyloxy) succiminide. First, the surface of titanium was treated with *n*-octadecyltrimethoxysilane (ODS), followed by cleaning with an eximer lamp. An aqueous photo-reactive gelatin solution (1 mg/ml) was cast onto the Ti surface treated with ODS and air-dried at room temperature. Subsequently, the plate was covered with a patterned photomask and was UV-irradiated for 10 s. The plate was washed thoroughly with cold distilled water, by which a micro-pattern of gelatin was formed. Monkey epithelial cells COS-7 and mouse fibroblastic cells STO were cultured on the pattern-immobilized plate. A significantly higher cell attachment was found on gelatin-immobilized regions than non-immobilized regions. It was concluded that the growth of cells on titanium was regulated by immobilized gelatin.

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