chapter 7

GENERAL DISCUSSION
COMPOSITE BIOMATERIAL MEMBRANES FOR BONE AUGMENTATION

Bone mass deficiencies are commonly encountered during surgeries to place dental implants. Manifestations of such deficiencies range from dehiscences and/or fenestrations in alveolar bone around placed dental implants to insufficient alveolar bone that is too narrow and/or too low to provide enough mechanical support and osseointegration to a dental implant. Different augmenting procedures are carried out to correct bone mass deficiencies according to different manifestations(1). Dehiscences and/or fenestrations that lead to exposure of dental implant threads can be treated using a surgical technique called guided bone regeneration. During guided bone regeneration, the dehiscences and/or fenestrations are covered either with barrier membranes alone or with barrier membranes in combination with bone grafting materials(2). When the alveolar bone of the patient has been resorbed extensively due to progressive periodontitis or alveolar atrophy after teeth extraction, an augmentation with bone grafts and/or bone graft substitutes is necessary. In such augmentation procedures, barrier membranes are also frequently used(3). In Chapter 2, an overview is presented to discuss barrier membranes that are currently being used in clinical practices or are under development for bone augmentation before or concomitantly with dental implant placement. Ideal synthetic barrier membranes should ensure biocompatibility, provide a delicate balance between good mechanical properties to maintain sufficient space for new bone formation and easy manageability to shape the contour of the jawbone well, and they ought to be user-friendly. Judging from the review, barrier membranes for the abovementioned individual indications still do not exist and call for further research and development.

Space maintaining properties are important for the barrier membranes used in guided bone regeneration, because new bone formation in bone defects requires sufficient space(4). Although being more rigid than poly(trimethylene carbonate)(PTMC) membranes(5), PTMC-biphasic calcium phosphate(BCP) composite membranes invaginated into the defects from both sides, contacted each other, and were not able to keep the space open at 12 weeks after implantation in the study described in Chapter 3. No new bone was found in the defects covered with PTMC-BCP membranes at 12-week follow-up, while the defects covered with PTMC-BCP membranes for four weeks were completely bridged by de novo bone. The following two facts are extrapolated to explain such conflicting findings. First, the PTMC-BCP membranes were more prone to be influenced by masticatory forces from masseter muscles and changed their positions because the in vivo surface erosion procedure of PTMC matrices liberated BCP particles from the PTMC-BCP membranes and roughened the membrane surfaces. Second, compared to the size of bone defects (5mm), the size of PTMC-BCP membranes (8 mm) may not have been large enough given the membranes were not fixed in place and their surfaces got roughened during degradation.

The dislocation of PTMC-BCP composite membranes and the foreign body reaction towards them also appeared in the study where they were used to preserve block autologous
bone grafts for onlay bone augmentation (Chapter 4). It is to prevent resorption of grafted bone blocks that barrier membranes are used to cover block autologous bone grafts.

The PTMC-BCP composite membranes did not interfere with the integration of the autologous bone graft blocks to the underlying recipient bone. Neither did the PTMC membranes or the membranes currently used in clinical practices. The transplanted autologous bone graft blocks became well integrated with the underlying recipient bone via maturing newly formed bone, and the bone blocks remained intact during the study. Instead, the underlying recipient bone tissue was gradually resorbed, echoing previous findings (6, 7). This study raises the question whether barrier membranes are needed to cover block bone grafts for preservation. If properly fixed to underlying bone, resorption of block bone grafts appears to depend on whether the grafts experience mechanical loading or not. No loading results in resorption, while loading results in preservation of bone mass (Wolff’s law) (8). Despite the foreign body reaction, the negligible influence of PTMC and PTMC-BCP membranes on the volume of the block autologous bone grafts indicates that these membranes can be useful for keeping particulate bone grafts or bone graft substitutes in place.

**COMPOSITE BIOMATERIALS FOR CRANIAL DEFECT RECONSTRUCTIONS**

Calcium phosphate bioceramics have been shown to be effective in reconstructing cranial defects clinically and the defects filled with hydroxyapatite granules or scaffolds are usually filled with a mixture of regenerated bone and remnant hydroxyapatite. Given the curved skull contour, brittle calcium phosphate bioceramics are hard to work with. Composite scaffolds made of synthetic biodegradable polymers and calcium phosphate bioceramic particles seem to be a promising solution to resolve this problem. Meanwhile, clinicians are seeking ideal implants that will be completely replaced by regenerated bone.

It was observed in Chapter 5 and Chapter 6 that the incorporated calcium phosphate bioceramic particles did not seem to execute the anticipated effects of promoting or inducing new bone formation when porous PTMC-calcium phosphate composite scaffolds were implanted in cranial defects or in paraspinal muscles in sheep. It was probably because the amount of calcium phosphate particles in the porous composite scaffolds was too low. In our studies, PTMC matrix took up 70% of the total volume and the 30% (v/v) calcium phosphate particles got sparsely dispersed in the PTMC matrices before composite scaffolds with 70% porosity were created. Cao and Kuboyama reported that filling critical sized bone defects in medial epicondyles of rat femurs with porous poly(glycolic acid)-β-TCP composite scaffolds at a weight ratio of 1:3 resulted in defect reconstructions comparable to filling the defects with clinically used HA scaffolds (9). Verheyen et al. inserted poly(L-lactic acid)-HA composite cylinders containing 50 wt% of HA particles into large transcortical defects in goat femoral diaphyses for three months and observed good bone binding between the implants and the defects via a mixture of woven and lamellar bone (10). To study osteoinductive
capacities of novel biomaterials, Hasegawa et al. implanted cylindrical porous scaffolds of 30 wt% poly(D,L-lactic acid) and 70 wt% uncalcined HA in dog dorsal muscles and observed ectopic new bone formation from two months of implantation on (11). Barbieri et al. showed in their comparative study that at least 40 wt% of nano-sized uncalcined HA is needed to induce new bone formation in dog dorsal muscles (12). Danoux et al. developed composite implants composed of a pair of dense extruded composite plates consisting of poly(D,L-lactic acid) and nano-sized hydroxyapatite particles at a 1:1 weight ratio and a 0.5 mm spacer between the plates serving as artificial pores. The composite implants induced new bone formation in the implants, especially near the artificial pores, when the composite implants were implanted in dog dorsal muscles (13). Judging from the successful examples, it is reasonable to expect that increasing the amount of calcium phosphate particles in PTMC-calcium phosphate composite scaffolds may improve their osteoconductive and/or osteoinductive properties.
REFERENCES


