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## **Preparation of chitosan-siloxane porous hybrids with hydroxyapatite for repair of skull defect**

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A craniotomy is performed for various neurological diseases, injuries, or conditions such as brain tumors, hematomas, aneurysms, and skull fractures. First, the small-sized holes, called "burr holes" were made to insert some surgical tools such as a shunt, a drain, an intracranial pressure monitor, and endoscope, etc. or be the starting point of removing large skull fracture. After surgery, the holes should be closed by the calcium phosphate cements or the titanium plates, because the skull defects are not spontaneously regenerated.

Calcium phosphate cements (CPCs) have attracted great interest as bone substitute material. However, the cements easily flow into the brain when they are contacted and mixed with cerebrospinal fluid or blood. On the other hand, the titanium plates cause the thinning of the scalp and sometimes come out on the surface. Moreover, they interrupt the observation of affected part by MRI. Therefore, new bone substitute materials for the burr hole were required.

Porous scaffold materials are necessary for the regeneration of new tissues in the tissue engineering field. High porosity is required for the tissue engineering scaffold in order to provide sufficient space for cell adhesion / proliferation, and to supply oxygen and nourishment. Chitosan-siloxane hybrids incorporated with calcium ions showed good osteocompatibility and formed apatite into alkaline phosphate solution. In this study, the porous hybrids with hydroxyapatite were implanted into the beagle skull bone defect and examined the bone regeneration.

Chitosan was dissolved in 0.25 M acetic acid to obtain 2 (w/v)% chitosan solution. GPTMS and  $\text{CaCl}_2$  of predetermined quantity were added into the chitosan solution and stirred at room temperature for 1 hour. The obtained solutions were poured into a plastic container, and stood overnight. It was then frozen at  $-20^\circ\text{C}$ , and lyophilized with the freeze-dryer. The obtained samples were soaked in 0.01 M  $\text{Na}_2\text{HPO}_4$  at  $80^\circ\text{C}$  for 3 days. The hybrids were washed with distilled water and then freeze-dried again. The surface analysis of the samples was examined by thin film X-ray diffraction (TF-XRD) and scanning electron microscopy (SEM). The samples for in vivo animal test were sterilized by  $\gamma$ -ray irradiation. The samples were implanted into the skull bone defect of adult female beagles. After several periods, the bone tissue surrounding the implanted site was examined histologically.

The chitosan-siloxane porous hybrids with hydroxyapatite by soaking in phosphate solution maintained their high porosity and water uptake property. The hybrids were degraded completely after 1 year implantation. The hybrids with hydroxyapatite accelerated the calcification compare with the only hybrids.