学 位 論 文 の 要 旨

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学 位 論 文 名　Bioactive Regeneration Potential of the Newly Developed Uncalcined/Unsintered Hydroxyapatite and Poly-l-Lactide-Co-Glycolide Biomaterial in Maxillofacial Reconstructive Surgery: An In Vivo Preliminary Study

発 表 雑 誌 名（巻，初頁～終頁，年）　Materials (14, 2461, 2021)

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論 文 内 容 の 要 旨

INTRODUCTION

Bone-fixation devices are essential instruments in the daily operation of oral and maxillofacial surgical practices. Accordingly, the materials used to manufacture bone plates and screws play an important role in the development of this field as well as other skeletal surgical specialties. Titanium has long been used to stabilize bone fragments, with excellent outcomes, and has therefore become the standard bone hardware material.

The ideal artificial material for maxillofacial bone fixation should have 1. adequate strength, 2. adequate time for resorption, and 3. osteoconductive ability. A novel bioabsorbable bone fixation material, unfired hydroxyapatite/poly-L-lactic acid/polyglycolic acid composite (u-HA / PLLA / PGA), is currently used for the treatment of maxillofacial bone fractures and jaw deformities. However, there have been no reports comparing the osteoconductive and biodegradability properties of u-HA / PLLA / PGA with those of previously used materials. In this study, we compared the bioactivity of u-HA / PLLA / PGA with that of u-HA / PLLA.

u-HA/PLLA/PGA theoretically has a shorter resorption time than u-HA/PLLA, there may be an increase in the number of biodegradation products, which could induce inflammatory reactions in the host after implantation in the maxillofacial region. However, to our knowledge, there have been no previous studies on the role of periosteum in the presence of composite implants consisting of u-HA particles, the biocompatibility of the new material, or its

degradation time in vivo.

We conducted a preliminary study with three main objectives: first - to assess periosteum-derived bone regenerative responses to u-HA/PLLA/PGA in rat mandibles via the presentation of periostin, a key extracellular matrix component of the periosteum involved in periosteum-derived bone-regenerative functions, and to compare this with the responses to u-HA/PLLA; second - to evaluate and compare the inflammatory responses to u-HA/PLLA/PGA and u-HA/PLLA in terms of CD68 expression; and third - to preliminarily measure and compare the degradation of these materials based on their molecular weight retention rates.

MATERIALS AND METHODS

We used a rat mandible model to compare the above features in u-HA/PLLA/PGA and uncalcined/unsintered HA and poly-L-lactic acid (u-HA/PLLA). We divided 11 male Sprague–Dawley rats into 3- and 16-week groups. In each group, we assessed the characteristics of a u-HA/PLLA/PGA sheet covering the right mandibular angle and a u-HA/PLLA sheet covering the left mandibular angle in three rats each, and one rat was used as a sham control. The remaining three rats in the 16-week group were used for a degradation assessment and received both sheets of material as in the material assessment subgroup. Specimens containing material sheet collected from the groups at Weeks 3 and 16 were decalcified, dehydrated, and embedded in paraffin. The specimens were sectioned along the coronal plane to produce each final section and then stained with HE for histological evaluation. HE staining and immunohistochemistry using Runx2, OCN, Periostin, and CD 68 antibodies were performed. All experiments with animals in this study were approved by the Animal Care and Use Committee of Shimane University.

RESULTS AND DISCUSSION

At 3 and 16 weeks after surgery, the rats were sacrificed, and mandible specimens were subjected to micro-computed tomography, histological analysis, and immunohistochemical staining. The results indicated that the interaction between the periosteum and u-HA/PLLA/PGA material produced significantly more new bone regeneration with a lower inflammatory response and a faster resorption rate compared to u-HA/PLLA alone.

The micro-CT images and HE staining showed that bone was added around both materials over time. On the other hand, the expression of Runx2, an osteoblast differentiation transcription factor marker, and Periostin, a periostcal-derived pre-osteoblast marker, did not differ significantly between the two materials, but both decreased over time. OCN expression, a marker of mature osteoblasts, and CD68, an inflammatory cell marker, showed no significant differences over time or between the two materials. On the other hand, the residual fraction of transplanted

material at 16 weeks after transplantation was significantly decreased in the u-HA / PLLA / PGA group.

CONCLUSION

The results of the present study indicated that the regenerative bone interaction between the periosteum and the new u-HA/PLLA/PGA material is beneficial for maxillofacial reconstruction, with a significant amount of bioactive-osteoconductive new bone regeneration. u-HA/PLLA/PGA shows great potential as a rapidly bioresorbable material with high biocompatibility and a low inflammatory response. These features may render this new biomaterial an ideal choice for reconstructive surgery of the midfacial region.