



Evaluation of Bone Regeneration Effect of Porous Carbonate Apatite in 3-wall Dehiscence Bone Defects in Dogs

Yusuke Shigemitsu, Nagomi Kitamura, Yusuke Sakaguchi, Katsuyuki Yamanaka, Takuya Sato.

R&D Department, GC Corporation, Tokyo, Japan



INTRODUCTION

Inorganic component of human bone is carbonate apatite (CO_3Ap) containing 4-8wt% of carbonate ion which is known as key element for bone remodeling. We have developed the synthetic CO_3Ap bone graft substitute (Cytrans[®] Granules) and confirmed the efficacy through clinical trial conducted in Japan^[1,2]. In addition, the CO_3Ap bone graft has been improved by increasing the porosity which cells could go through. In this study, we evaluated the efficacy of porous CO_3Ap compared to dense CO_3Ap in a dog model.

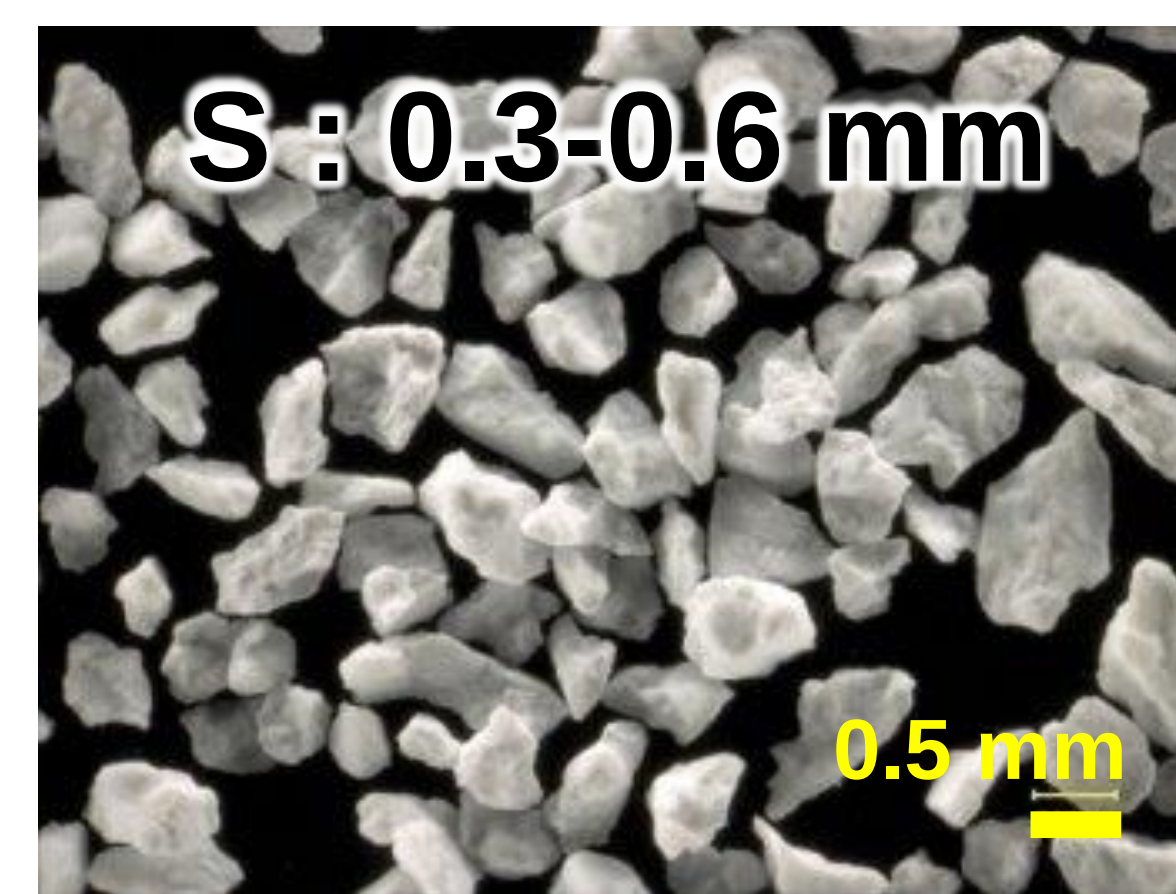
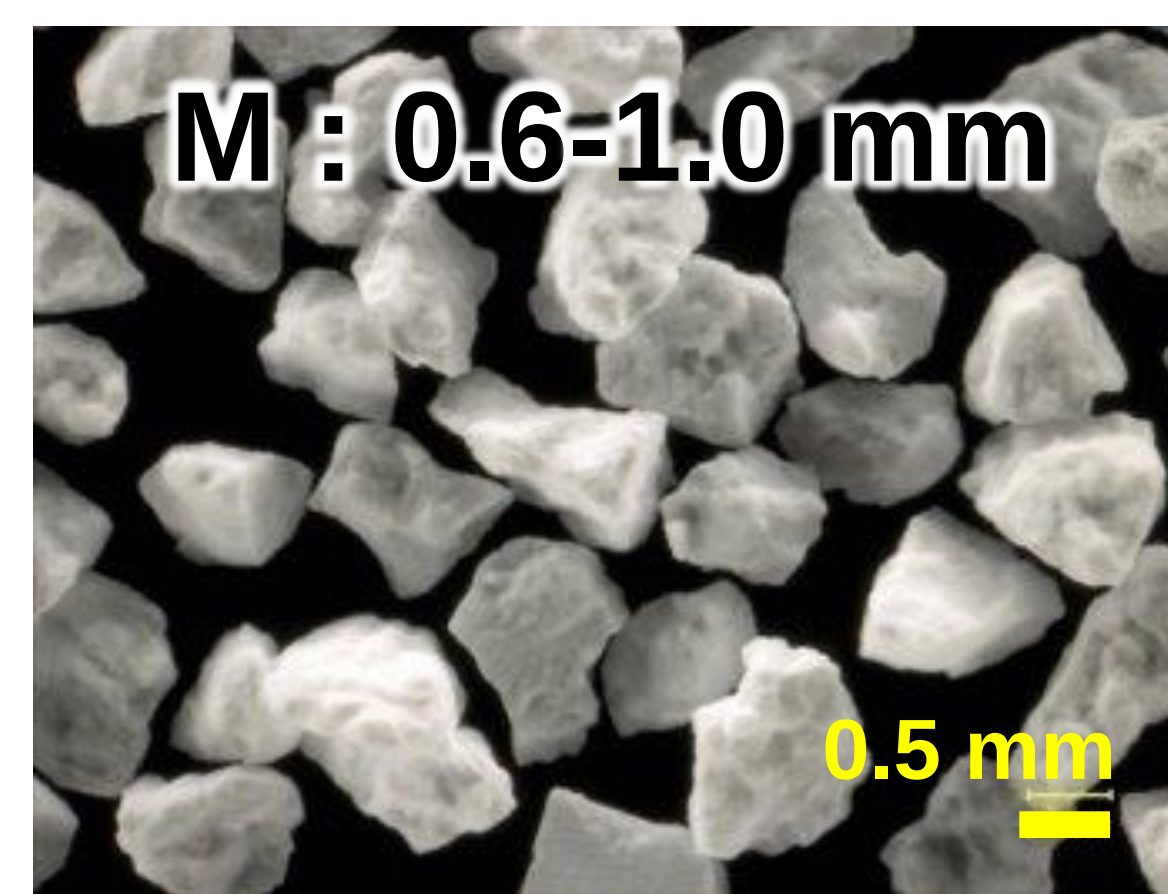
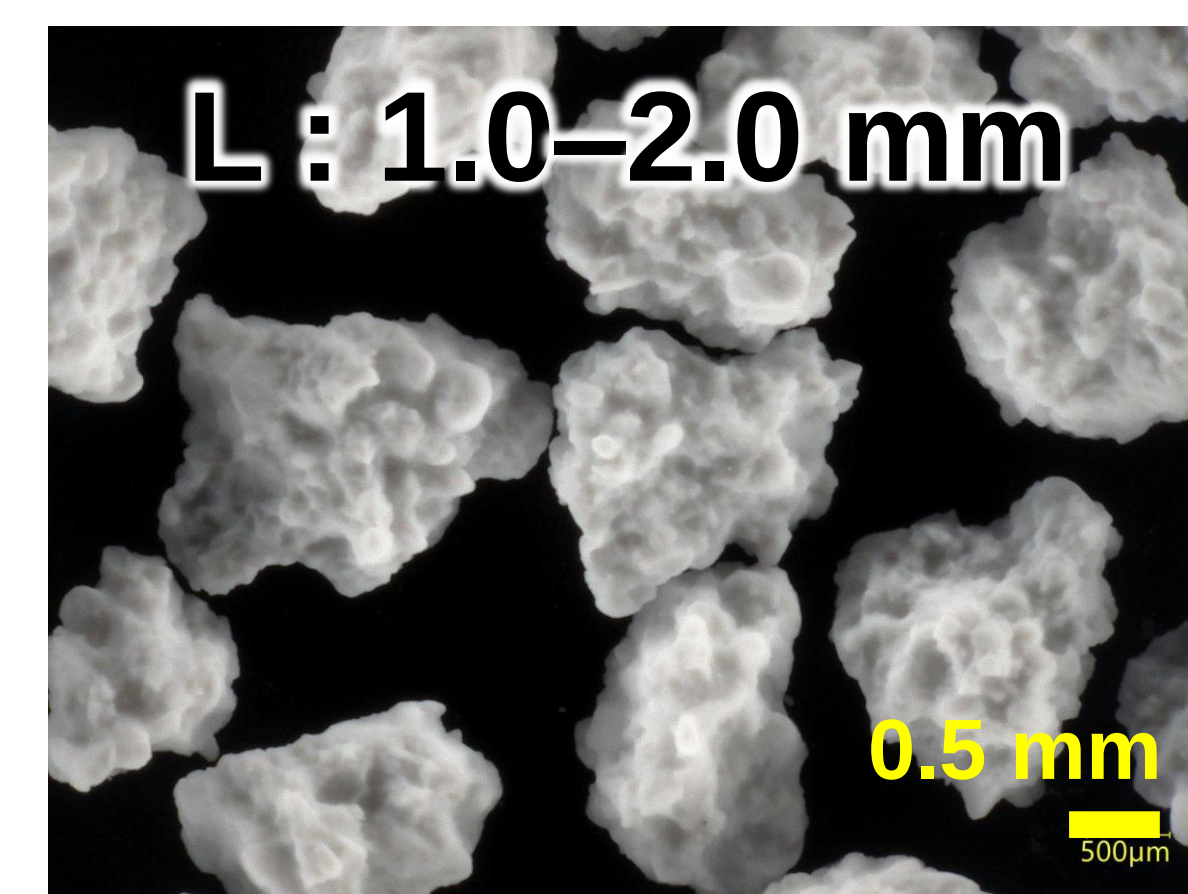
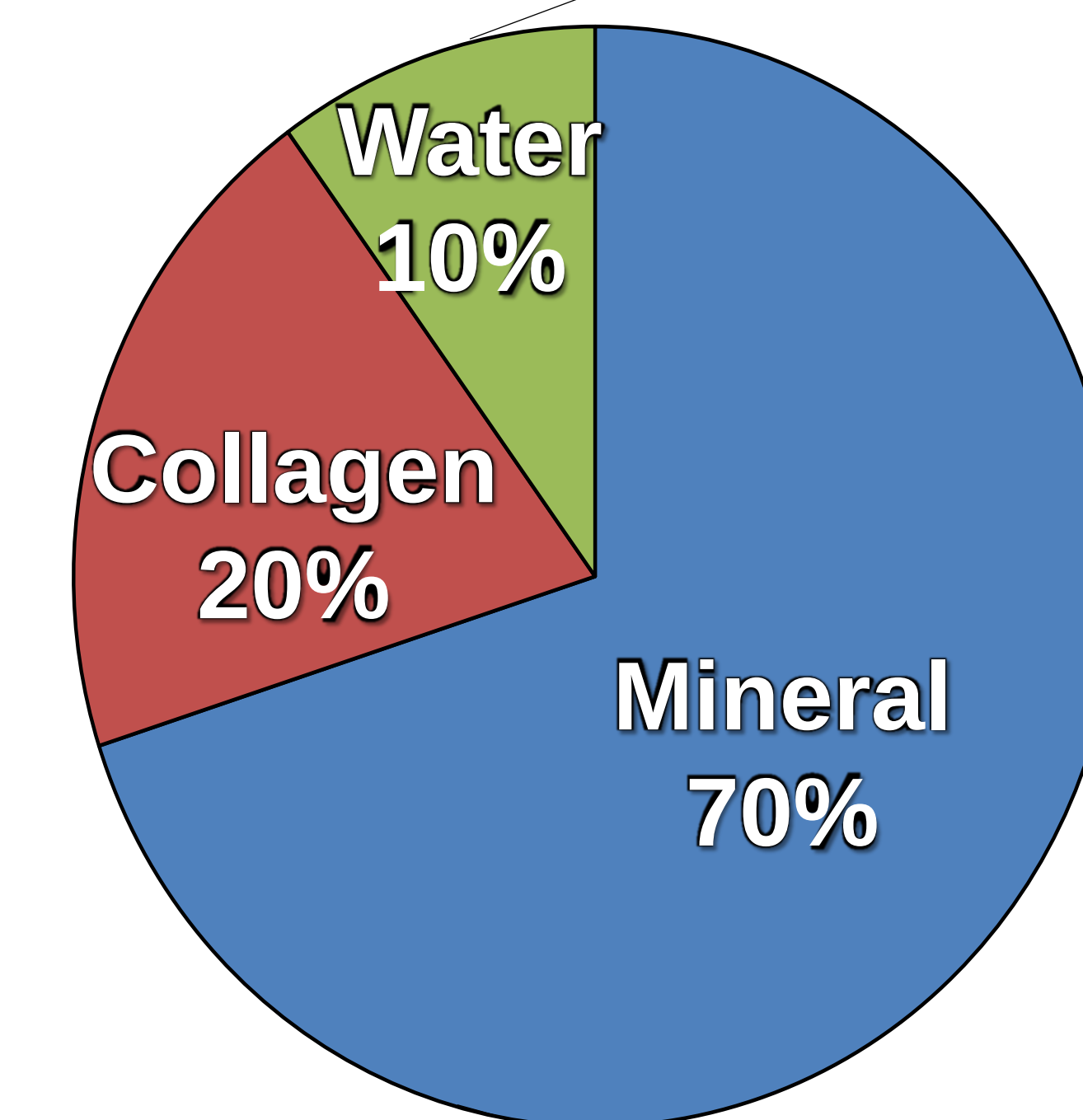


Table 1. Composition of bone. ^[3]



Component	Contents (wt%)
	Human bone
PO_4^{3-}	46.6
Ca^{2+}	34.8
CO_3^{2-}	7.4
Na^+	0.9
Mg^{2+}	0.72
Cl^-	0.13
K^+	0.03
F^-	0.03

Figure 1. Carbonate apatite bone graft substitute (Cytrans[®] Granules).

[1] Kudoh K, *J Oral Maxillofac Surg.* **2019**, 77, 985.

[2] Nakagawa T, *J Periodontal Implant Sci.* **2019**, 9, 382.

[3] LeGeros RZ, *Monographs in Oral Sci.* **1991**, 15, 201.



Materials

Sample	Composition	Structure
Dense CO ₃ Ap	CO ₃ Ap Same as bone mineral	Dense granule Similar to cortical bone
Porous CO ₃ Ap	CO ₃ Ap Same as bone mineral	Porous granule Similar to cancellous bone

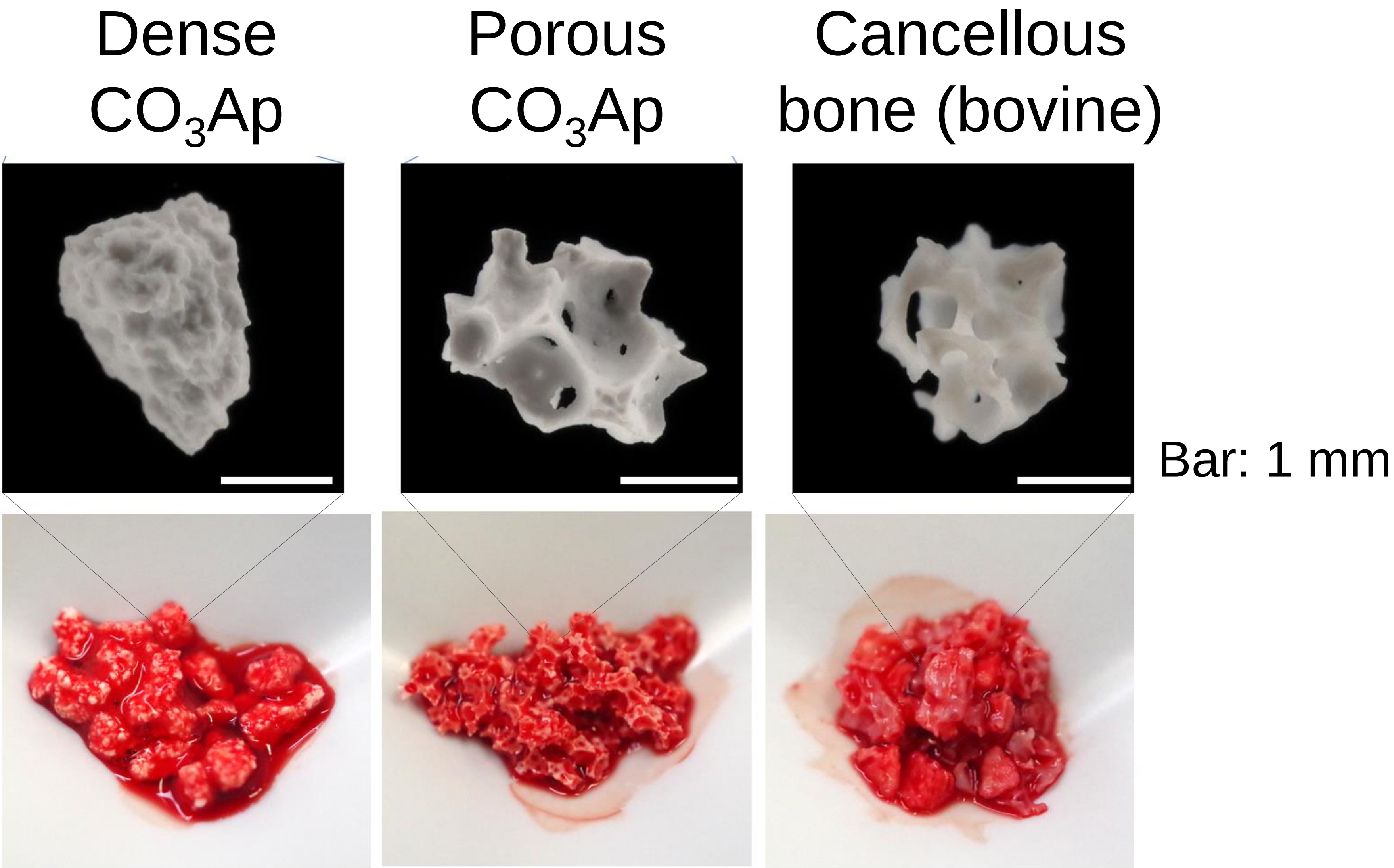


Figure 2. Microscopic image of samples.

Animal Study*

Lower premolars (P4) were extracted from adult dogs. After a healing period of 8 weeks, 3-wall bony defects (10 × 4 × 5 mm) were created at the proximal section of molars with buccal dehiscence. The defects were filled with 0.3 mL porous CO₃Ap (particle size: 1-2 mm), or dense CO₃Ap (particle size: 1-2 mm) and surgical incision was closed without using membrane. μ CT evaluation was performed at 12 weeks after healing.

*The experimental protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of Hamri Co., Ltd. (Ibaraki, Japan); approval number IACUC No. 18-H049, 19-H097.

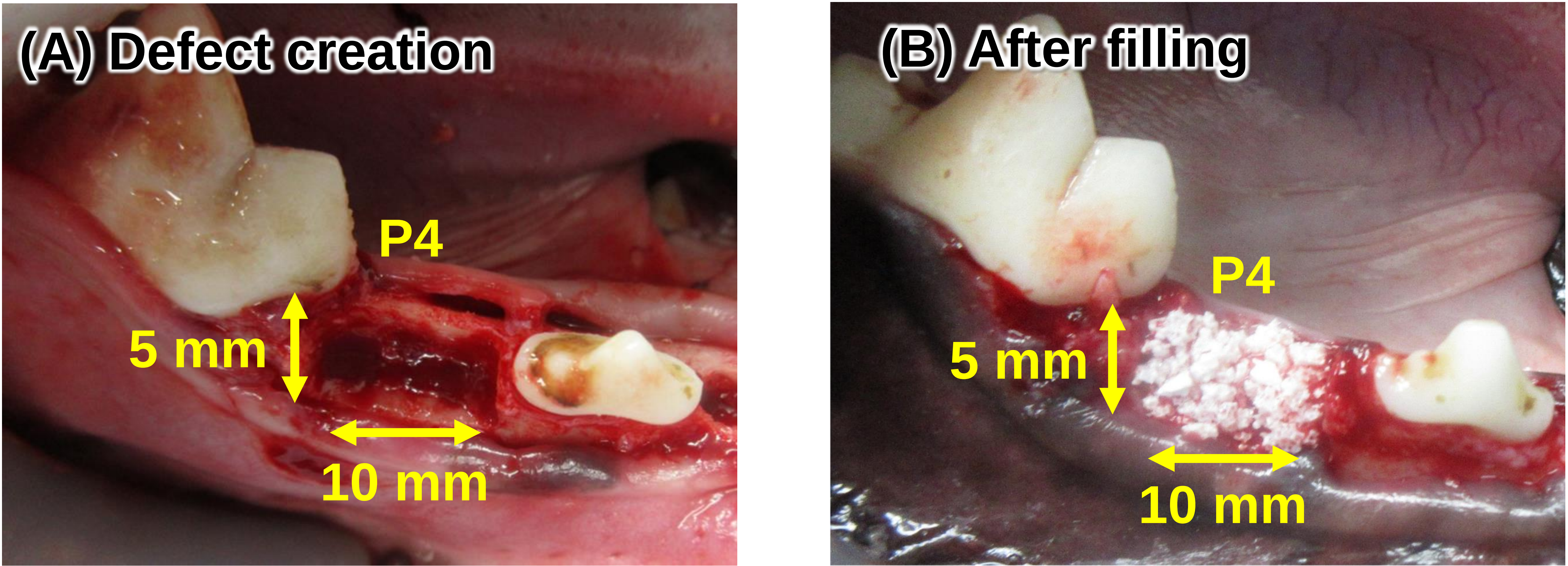


Figure 3. Defect creation in dog mandibular bone

Clinical Findings

There were no signs of inflammation, wound dehiscence, leakage of CO₃Ap, or infection in both groups.

μCT analysis

New bone formation throughout the defect were observed in porous CO₃Ap group, which were comparable to those in dense CO₃Ap group. Percentage of granules remaining in porous group was significantly lower than in dense CO₃Ap group.

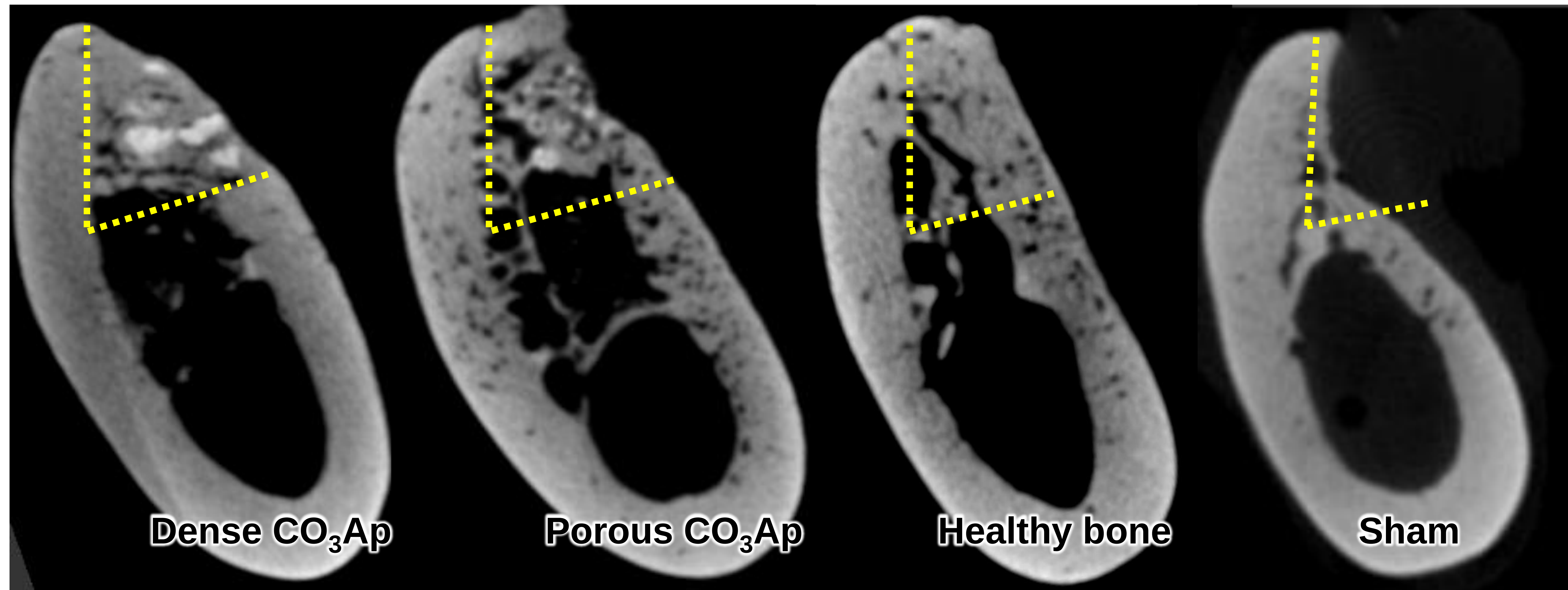


Figure 4. Representative μCT images of coronal sections

μCT analysis

Percentage of granules remaining in porous group was significantly lower than in dense group. Volume of the new bone formed was 0.24 mL in the porous group and 0.23 mL in the dense group, with no significant difference.

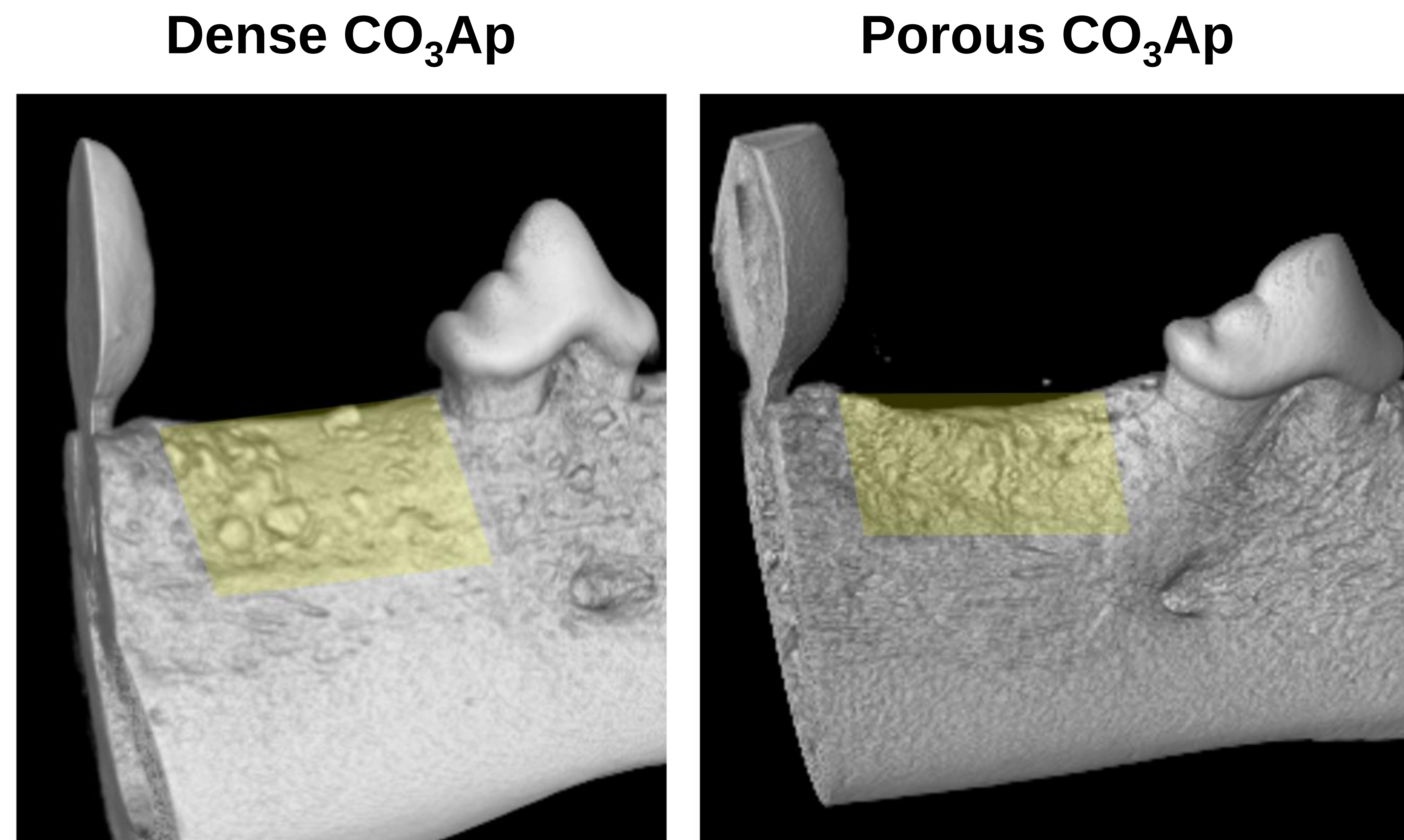


Figure 5. 3D constructed μCT image of healing site

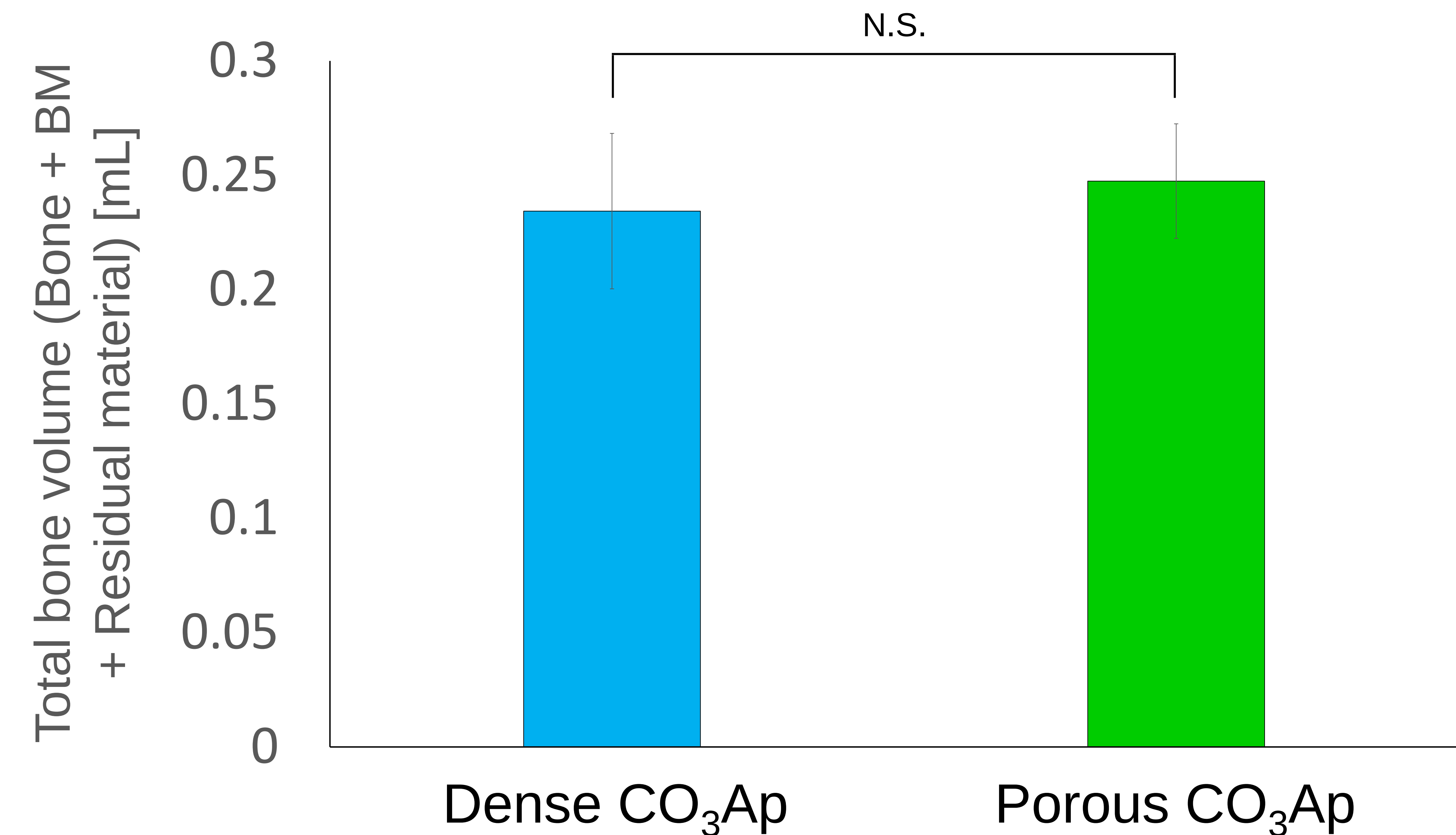


Figure 6. Volume maintaining capability (lateral bone volume).

Approximately 80% of the volume was maintained compared to 0.3 mL volume that was implanted. Volumetric changes were not significantly different among the two groups.

DISCUSSION

CO₃Ap granules were fabricated by compositional transformation based on dissolution precipitation reaction using low crystalline calcite granules as a precursor which is previously described^[4]. CO₃Ap granules will be replaced by newly formed bone through bone remodeling processes. Furthermore, the porous structure is expected to promote efficient bone formation by allowing cells to penetrate into the pores and promote angiogenesis and tissue regeneration.

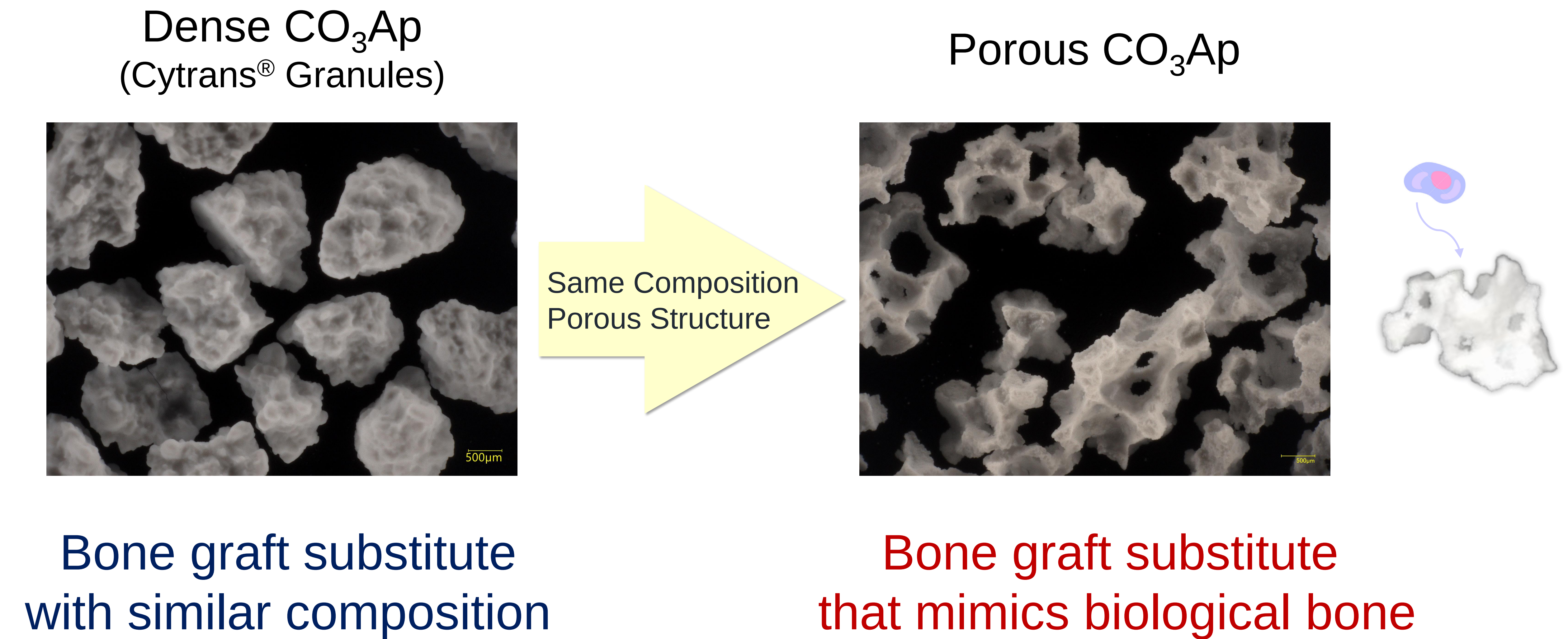


Figure 7. Comparison of dense and porous CO₃Ap.

CONCLUSION

Porous CO₃Ap showed no difference in bone formation and volume of new bone compared to the dense CO₃Ap. However, less material remained in the porous CO₃Ap, suggesting that porous CO₃Ap tended to promote bone replacement. These results suggest that porous CO₃Ap is a clinically useful bone graft substitute with excellent bone replacement potential.