Comparison of off-the-shelf β-tricalcium phosphate implants with novel resorbable 3D printed implants in mandible ramus of pigs

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Abstract

3D-printed patient-specific implants derived from CAD/CAM-based technologies are used in facial reconstructive surgery as an alternative to preformed bone graft substitutes. However, to minimize the invasiveness and long-term adverse effects of surgical interventions, the implant needs to exhibit exact fitting, porosity, density, and volume and be made from resorbable materials that allow ingrowth and formation of new bone tissue. Therefore, we present this pilot study using 3D-printed implants consisting of pure β-TCP, produced using a novel technique that assures these properties. Eight pigs received 3D-printed truncated porous cone bone implants paired with either an off-the-shelve chronOS (DePuy Synthes chronOS Vivify Preforms) preformed block (*n* = 4) or a no-implant void (*n* = 4) in a surgically created defect on each side of the angle of the mandible. After 6 months, CT data showed that all 3D-printed implants performed as well as the off-the-shelve implants, with predicted osteointegration medially and laterally and with minimal gapping between the implants and native bone. The CT findings were confirmed by histological analysis which revealed that the 3D-printed implants as well as the off-the-shelve implants were almost completely resorbed. Much of the resorbed volume had been replaced by vascularized compact bone, and fusion between newly formed bone and native bone was observed in all implants, further indicating that the 3D-printed implants and off-the-shelve implants performed equally well. Only soft tissue developed in the void control sites. Further studies are needed to confirm these initial findings.

Introduction

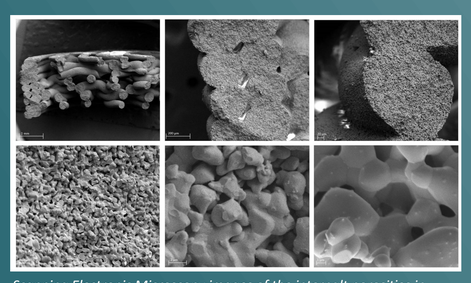
3D printed patient specific implants derived from CAD/CAM-based technologies are presented as an alternative to preformed bone graft substitutes. Yet, today, clinicians must still choose between patient specificity or implant properties that are favorable for bone remodeling, leading to off-the-shelf solutions such as the β-tricalcium phosphate granules and preformed blocks that are used today.

Ideal patient specific implants not only exhibit exact fitting, porosity, density, and volume but are also insoluble, osteoconductive, osteoinductive, have resorption properties that resemble native bone, and allow ingrowth and formation of new bone tissue.

Using Ossiform's proprietary technology it is now possible to 3D print bioceramics composed of β-tricalcium phosphate, resulting in a structure which meets all of the abovementioned requirements and thereof the making of P3D Bone. Although initially used *in vitro*, several studies have investigated the resorbable properties of the P3D Bone *in vivo* with promising results (**Jensen 2020**, **Jensen 2018**, **Slots 2017**). In this pilot study, the 3D printed P3D Bone has been directly compared to a commercially available preformed β-tricalcium phosphate implant in relation to defects in the mandible ramus of pigs. The aim of the study was to analyze the performance of the implants that fulfill the aforementioned requirements in a clinically relevant implantation model where the implant, defect and bone are similar in size to what would be expected in human patients.

The technology

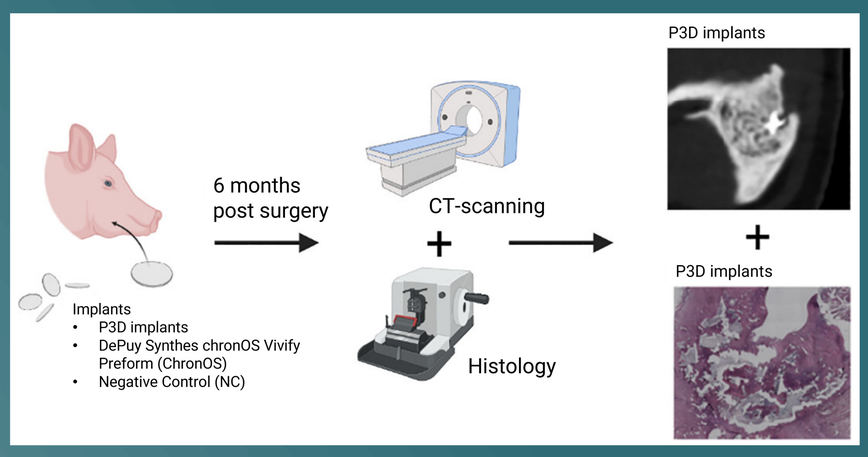
Our proprietary technology allows us to produce patient specific implants composed of β-tricalcium phosphate by combining β-tricalcium phosphate with a fatty acid resulting in a 3D printable paste. Subsequent sintering completely removes all fatty acids from the implants resulting in a porous and spongious bioceramic implant.



Scanning Electronic Microscopy images of the internalt porosities in P3D Scaffolds at different magnifications

Experimental setup

Eight pigs were anesthetized, and a predetermined hole was dissected in the mandible in each side of the pig. Hereafter, the P3D Bone implant was inserted on one side. On the other side, either the control implant was inserted, or the hole was left as a void. The pigs were stabled individually for six months before evaluating the performance of the implants by CT-scanning and histology of jaw sections



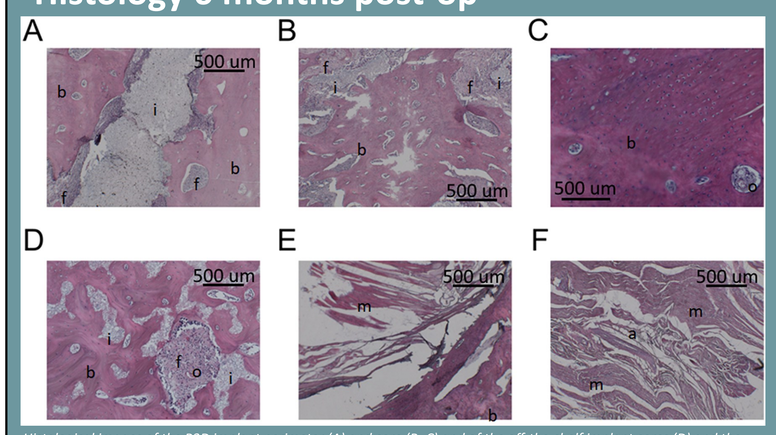
Results

Six months after the surgical procedure, the pigs were CT-scanned, and the CT images analyzed. The analysis showed various degrees of integration, resorption, and ossification of the voids – furthermore, bone integration and ossification at the perimeters and middle of the P3D Bone implant resembled natural bone presenting a cortical surface and spongious-like bone within the implants.

The findings from the CT-scan were supported by the histological analysis which showed that most of the P3D Bone implant was resorbed leaving only a few and small pieces of the original implant. As β-tricalcium phosphate does not degrade on its own inside the body, it is likely that the disappearance of the implants after six months is due to resorption by osteoclasts.

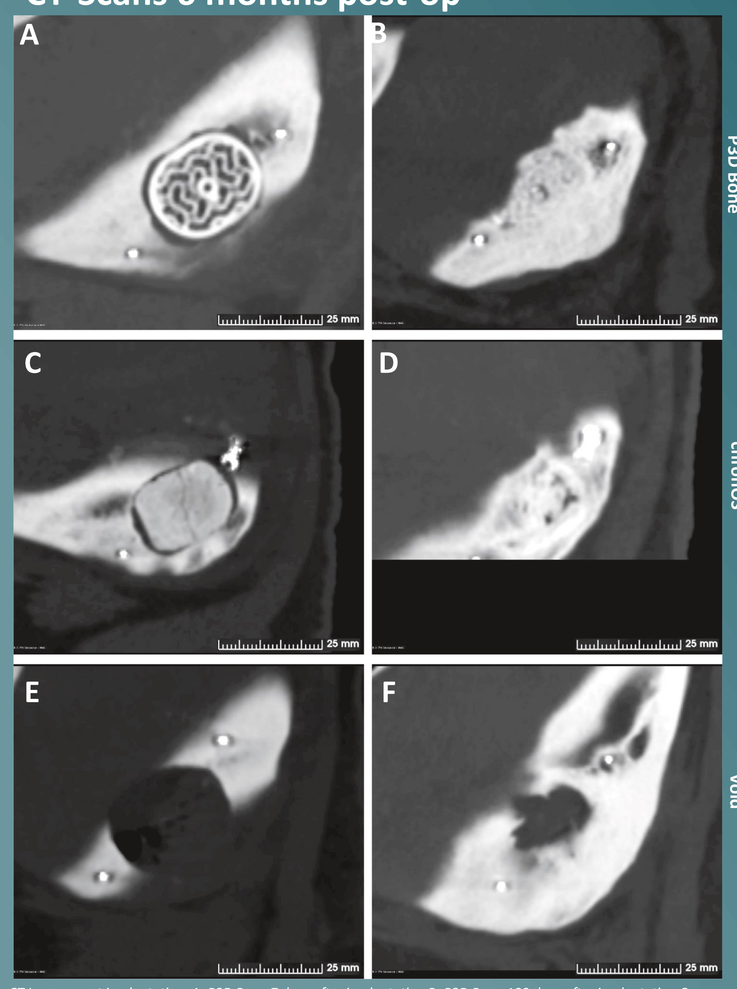
The histology slides also revealed that the inside of the P3D Bone implants was filled with soft tissue, muscle tissue and bone tissue, with bone tissue being dominant. The bone tissue was dense with small canals of soft tissue containing blood vessels, and comparison of the P3D Bone implant site with native bone suggested that the newformed bone was mature. Meanwhile, the negative control voids were filled with adipose tissue, fibrous/connective tissue, and muscle tissue with no bone tissue.

Histology 6 months post-op



Histological images of the P3D implant perimeter (A) and core (B–C) and of the off-the-shelf implant cores (D) and the resected non-treated voids (E–F) after 6 months . The images were all recorded using a ×4 objective except for C, which was recorded using a ×10 objective. (b): Bone. (f): Fibrous/connective tissue. (m): Muscle. (a): Adipose tissue. (i): Implant.

CT-Scans 6 months post-op



CT Images post implantation. A: P3D Bone 7 days after implantation B: P3D Bone 180 days after implantation C: ChronOS 7 days after implantation D: ChronOS 180 days after implantation E: Void 7 days after implantation F: Void 180 days after implantation

Conclusion

The study showed that the P3D Bone implants performed at least equally as well as the commercially available off-the-shelf implants while also being patient specific and that newly formed mature bone was integrated within the implants after six months. Furthermore, the study showed that the P3D Bone implants are highly biocompatible and supports natural cellular and systemic responses.

Future perspectives

The fatty acids used in the fabrication of the P3D Bone can function as a vessel for relevant pharmaceuticals. By incorporating one or more pharmaceuticals in the P3D Bone patients could receive a patient specific, fully resorbable implant which doubles as a local therapeutic treatment, allowing chemotherapy, antibiotics, or bone stimulants to act at the damage/implant site, resulting in lower risks of cancer recurrence and biofilm formation or a faster and more complete regeneration of the bone. So far, preliminary in vitro and in vivo studies have shown promising results, but further studies are needed prior to entering the pre-clinical stage .

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