

Evaluation of BONIT[®], a fully Resorbable CaP Coating Obtained by Electrochemical Deposition, after 6 Weeks of Healing: A Pilot study in the Pig Maxilla

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Abstract

The present pilot study reports on the evaluation of BONIT, a fully resorbable CaP coating obtained by electrochemical deposition, in a pig model in the maxilla. Control implants were \varnothing 4.9 mm x 8 mm titanium plasma-sprayed (TPS) and test implants were further coated by a 15-20 μ m thick BONIT layer. The coating was found to be mainly Brushite ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$), its Ca/P was 1.1 ± 0.1 . By 6 weeks of healing, all implants osseointegrated. Bone apposition at the test and control groups was respectively 73.0 ± 6.2 % and 49.8 ± 16.4 % ($p = 0.009$). The bioactive coating induced a pronounced osteoconductive effect with remarkable new bone apposition in the spongy bone between the implant threads. The coating was resorbed by > 99 % and was substituted by bone. Macrophagic or osteoclastic activity was not found at the interface whereas it has been reported for resorbing plasma-sprayed CaP coatings. The results suggest that fully resorbable CaP coatings might be able to replace plasma-sprayed HA coatings as the second generation of bioactive coatings.

Introduction

CaP coatings have been in use in the dental and orthopedic fields for several years. CaP coatings on bioinert materials have been advantageous in case of osteoporosis, gap crossing and bone grafting [1]. They are more predictable in poor bone quality [2] and enhance tolerance to deleterious micromotion [1,3]. Long-term concerns, however, have been raised for plasma-sprayed (p-s) HA-coated implants, that may challenge the short-term achievement : 1) they may flake, 2) the coating-substrate interface strength decreases after functional loading [4], 3) the dissolution extent of the coating is unpredictable [5,6], 4) little is known about the maintenance of osseointegration in case of total dissolution of the p-s HA-coating [6], 5) HA-coatings may induce dramatic bone loss in case the HA-coating is contaminated by plaque [7,8].

The best way to eradicate every concern about the mid- and long-term performance of a bioactive coating would be to use fully resorbable bioactive materials. The latter have been investigated by few authors [9-13]. Plasma-spraying and physical vapor deposition (PVD) have been tried to obtain resorbable HA coatings. Maxian et al. [10] reported on a 60 % crystalline p-s HA that was resorbed in a rabbit model after 12 weeks but results could not be replicated in the dog model [13]. The PVD method allows for a thin amorphous HA coating in the 0.5-5 μ m range that resorb too fast [14] to initiate the bioactive response, or when converted into crystalline HA is not fully resorbable [14]. Supporting the concept of resorbable bioactive coatings, our approach had been different [12]. We

sought for resorbing coatings, in the 10-30 μm range, without necessarily striving for HA as a coating substance. The BONIT coating, made of mainly Brushite and obtained by electrochemical deposition, represents an alternative to the HA p-s and PVD coatings [12]. It is obtained by a room temperature process that allows for complete coverage of complex shapes and porous surfaces. Its ca. 60 % porosity elicit for a further stuffing of active molecules like growth factors and/or antibiotics to increase implant predictability in sub-optimal bone or mechanical conditions.

Resorbing CaP-coatings have been documented to impede bone apposition at dissolving areas [1,3,10,15] and to attract macrophages and multi-nucleated cells [16,17]. Therefore, when full resorption of a bioactive coating is expected, its safety and efficacy should be assessed. The safety of the BONIT coating was investigated in a previous study after 12 weeks of implantation [12]. The coating was fully resorbed and was substituted by thin continuous trabecules of bone, leading to 60 % of bone-implant contact (BIC) in this poorly trabecular maxilla. Demonstration of its efficacy against a bioinert osteophilic surface like TPS was warranted. In addition, the question of how long is required for entire dissolution of the BONIT coating was also raised. Subsequently, evaluation of the coating after a shorter period was considered to be relevant. In this study, the first tested hypothesis was that, after 6 weeks of healing, the BONIT coating would increase the BIC when compared to the control implants. The second hypothesis was that the coating would have undergone an homogeneous partial resorption.

Material and Methods

A female farmer Land Race pig model was developed by Perrin et al. [non published]. This model offers the opportunity of placing 8-10 implants per hemi-maxilla and is therefore most suitable for pilot studies. The pigs are not sacrificed by the end of the experiment. The two-stage Pitt Easy Bio-Oss implant system (Oraltronic, Bremen, D) was used. TPS roughened implants \varnothing 4.9 mm x 8 mm served as control implants. The test implants were further coated with a 15-20 μm BONIT layer. Sample size for both groups was $n = 8$. The BONIT coating was obtained by a proprietary electrochemical deposition method (DOT, Rostock, D). This room temperature process allows for a non line-of-sight coverage, including hollow designs, micronic and sub-micronic surface irregularities.

Premolar extraction in the maxilla was performed providing a room of 90-100 mm for implant placement. After 3 months of healing, 8 implants were placed in each hemi-maxilla, 4 for the test and control groups, and were left to heal in a submerged fashion during 6 weeks. Implants retrieval with the surrounding bone was achieved by segmental osteotomy.

The samples were fixed, processed for histology and implants were sectioned in the mesio-distal plan. A central section of 30-50 μm for each implant was obtained and stained with toluidine blue, some of them with the von Kossa staining. The histomorphometric measurement was performed by the eye-grid method. The Wilcoxon rank test for non-parametrical data was used at the confidence level of $\alpha = 5\%$. EDS and XRD (SIEMENS 8000) were used for physico-chemical characterization of the resorbable coating.

Results

The structure of the BONIT layer was similar to Brushite, $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ (JPDCS 9-77). The Ca/P ratio was 1.1 ± 0.1 , meaning that another phase was present. Figure 1 shows the BONIT coating surface at x 400. Packed 10-20 μm plates of Brushite, were found, following a repetitive motive.

All implants osseointegrated, a control implant showed inflammation and was excluded from analysis. The BIC for the BONIT and the TPS groups was $73.0 \pm 6.2\%$ and $49.8 \pm 16.4\%$. The difference was statistically significant ($p = 0.009$) and confirmed the 1st hypothesis. At the BONIT coated implants, extensive new bone apposition was found at the spongy level, specially between the threads at the screw core (fig. 2), showing the osteoconductive capacity of the coating.

By 6 weeks of implantation, the bioactive BONIT layer was resorbed. In 2 slices only, minute spots of remaining BONIT could be seen (fig. 3), leading to a resorption rate of $> 99\%$. Macrophages or multi-nuclear cells were not seen at the interface or near the coated implants.

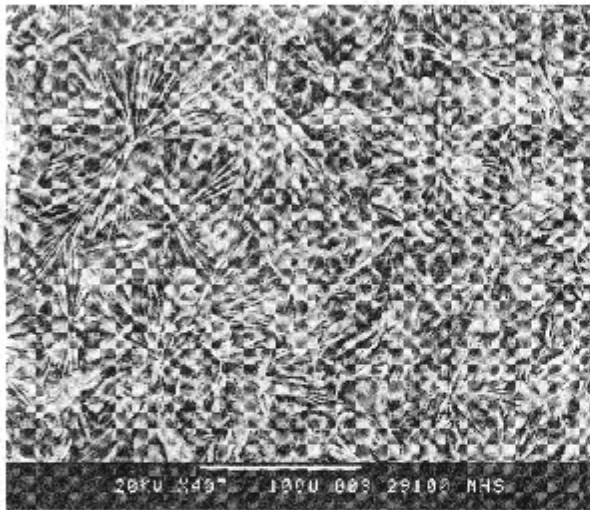


Fig 1: SEM micrograph of the BONIT coating at x 400

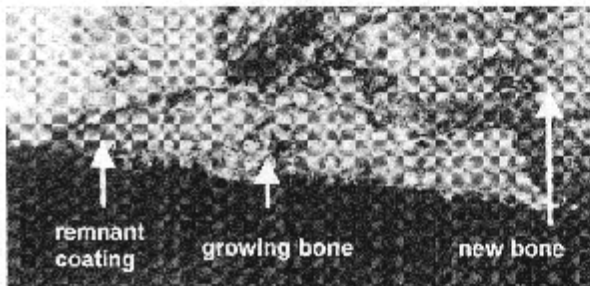


Fig 3 : Detail of a remnant coating spot. Bone (von Kossa stained, small arrow) is growing from the middle of the coating, resorbing it. Original mag. X 40

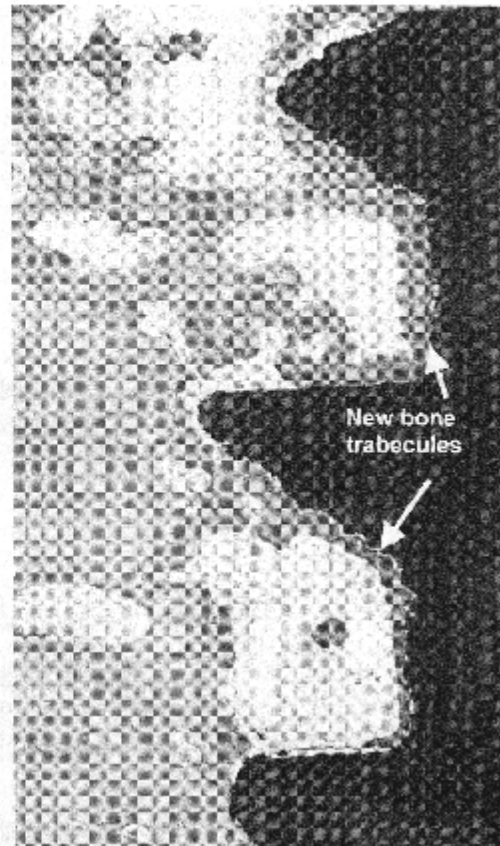


Fig 2 : Osteoconductivity in the spongy bone between the threads at a BONIT coated implant. Original mag. X 20

At one of the remaining coating spots, bone was growing from the middle of the coating, at its expenses (fig. 3). These results disprove the 2nd hypothesis, that a partial homogeneous dissolution only would have occurred after 6 weeks of healing.

Discussion

The present study investigated, 1) the biologic response of the BONIT layer, 2) its efficacy to induce more bone apposition when compared to a TPS surface and 3) its resorption/substitution pattern. The coating was able after 6 weeks to induce a higher BIC (+ 23 %) with a lower standard deviation than the TPS surface which is yet an osteophilic surface. This was remarkable at the core level of the apical threads where bone had been removed during drilling at placement. The bioactive coating had a pronounced osteoconductive effect in the spongy bone as it induced more bone contact and more bone filling between the threads (fig. 2). This might be due to the capillary effect produced by the porous coating. Blood in contact with the resorbable coating is aspirated probably across its entire thickness, reaching eventually the underneath rough TPS coating. It may be that this allowed for a better wetting and further anchorage of the clot fibers into the open 3D structure of the coating. This could allow for a faster migration of the progenitor cells issued from the marrow space [18] and would explain the pronounced osteoconductive response. The enhanced BIC suggests that the BONIT coating on top of a TPS surface should allow for shorter healing periods than presently accepted, at least equivalent to the 6-8 weeks of delayed loading advocated for textured bionert surfaces [19,20], especially in spongy bone. Implementation of this coating should permit to shorten the duration of implant therapy and enhance the predictability of early and immediate loading protocols. Multi-center studies have been initiated with the presently used dental implant system to support these assumptions.

Few could be learnt from this study on the resorption/substitution pattern because the bioactive coating was fully resorbed except 2 minute spots displaying on-going resorption. The bone found in the middle of one of them (fig. 3) might be using the resorbable coating as a Ca and PO₄ ion source to grow directly at the coating expenses like in the Bone Metabolising Unit (BMU)-based remodeling. A removal activity of coating particles mediated by macrophages and multi-nucleated cells was often reported at resorbing p-s [16] or electrophoretic [17] bioactive coatings. However, these cells were not found at the BONIT coated implants, even at the remnant sites. This is suggestive of either an ionic dissolution process rather than a particle release one or an easy resorption of the coating plates by the phagocitizing cells. Finally, this study might also confirm that bioactive coatings do not need to further stay once osseointegration has been achieved [10,11].

Value of the BONIT coating should be most relevant at the short-term and specially at spongy bone sites like the posterior mandible and maxilla, when stimulation of osteogenesis is requested. This experiment has been successful in verifying it. At the longer term, the bone response difference between bioactive and bioinert surfaces are smoothed and rendered negligible [17,21]. In cortical bone, the benefit of bioactive layers seems unrelevant [22] while in spongy bone their advantages have been clearly asserted in vivo [6] as well as in clinical applications with short dental implants [2,23].

In conclusion, it appears that full resorption of the BONIT coating within 6-12 weeks is highly probable. The observed enhanced bone response suggests it should be able to replace advantageously the first generation of plasma-sprayed HA and reduce the duration of implant therapy. Further studies are warranted to confirm its efficacy in other applications and to gain a better understanding of the dissolution/substitution pattern of this fully resorbable coating.

References

1. K. Søballe, E.S. Hansen, H. Brockstedt-Rasmussen, C. Bünger, in *Hydroxyapatite Coatings in Orthopaedic Surgery*, R.G.T. Geesink & M.T. Manley (eds.), New York, Raven Press (1993), p. 107
2. A.P. Saadoun, M.L. Le Gall, *Int. J. Periodont. Rest. Dent.* 12 (1992), p. 487
3. S. Szmukler-Moncler, Y. Reingewirtz, H-P. Weber, in *Biological mechanisms of tooth movement & craniofacial adaptation*, Z. Davidovitch & L.A. Norton (eds.) Boston, Harvard Society for the Advancement of Orthodontics (1996), p. 611
4. I.M.O. Kangasniemi, C.C.P.M. Verheyen, E.A. van der Velde, K. de Groot, *J. Biomed. Mat. Res.* 28 (1994), p. 563
5. J.A. Janssen, J.P.C.M. van der Waerden, J.G.C. Wolke, *J. Biomed. Mat. Res.* 27 (1993), p. 603
6. H. Caullier, J.P.C.M. van der Waerden, J.G.C. Wolke, W. Kalk, I. Naert, J.A. Janssen, *J. Biomed. Mat. Res.* 31 (1997), p. 19
7. B.W. Johnson, *Calif Dental Ass J.* (1992), p. 33
8. S.L. Wheeler, *Int. J. Oral Maxillofac. Implants* 11 (1996), p. 340
9. D.R. Cooley, A.F. van Dellen, J.O. Burgess, A.S. Windeler, *J. Prosthet. Dent.* 67 (1992), p. 93.
10. S.H. Maxian, J.P. Zawadski, M.G. Dunn, *J. Biomed. Mat. Res.* 27 (1993), p. 617
11. J.A. Janssen, J.G.C. Wolke, S. Swann, J.P.C.M. van Waerden, K. De Groot, *Clin. Oral Implants Res.* 4 (1993), p. 28
12. S. Szmukler-Moncler, D. Perrin, A. Piattelli, A. Scarano, in *Biological mechanisms of tooth eruption, reabsorption and implant replacement*, Z. Davidovitch & J. Mah (eds.) Boston, Harvard Society for the Advancement of Orthodontics (1998) p. 481
13. H-P. Weber, M. Corso, C. Sirota, F. Rassol, D. Lee, S. Szmukler-Moncler, *Clin. Oral Implant Res.* 8 (1997), p. 434
14. T. Hakayawa, M. Yoshinari, K. Nemoto, J.G.C. Wolke, J.A. Jansen, *Clin. Oral Implants Res.* 11 (2000), p. 296
15. J.E. Dalton, S.D. Cook, *J. Biomed. Mat. Res.* 29 (1995), p. 329
16. C.P.A.T. Klein, Y.M.H.F. Sauren, W.E. Modderman, J.P.C. van der Waerden, *J. Appl. Biomater.* 4 (1994), p. 369
17. M. Gottlander, C. Johansson, A. Wennerberg, T. Albrektsson, S. Radin, P. Ducheyne, *Biomaterials* 18 (1997), p.551
18. J.E. Davies, *Int. J. Prosthodont.* 11 (1998), p. 391
19. R.L. Lazzara, S.S. Porter, T. Testori, J. Galante, L.A. Zetterquist, *J. Esthet. Dent.* 10 (1998), p. 280
20. D. Buser, T. Nydegger, H-P. Hirt, D. L. Cochran, L-P. Nolte, *Int. J. Oral Maxillofac. Implants* 13 (1998), p. 611
21. H Oonishi, M. Yamamoto, H. Ishimaru, E. Tsuji, S. Kushitani, M. Aono, *J. Bone Jt. Surgery* 71B (1989), p. 213
22. J.A. Janssen, J.P.C.M. van der Waerden, J.G.C. Wolke, *J. Biomed. Mat. Res.* 27 (1993), p. 603
23. E.R. Teixeira, M. Wadamoto, Y. Akagawa, T. Kimoto, *J. Prosthet. Dent.* 78 (1997), p. 166.

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