

Preparation of a Resorbable Osteoinductive Tricalcium Phosphate Ceramic

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Introduction

Over the past decade we have demonstrated numerous times that calcium phosphates can be rendered with osteoinductive properties by introducing specific surface microstructures¹. Since most of these calcium phosphates contained hydroxyapatite, they are either slowly or not resorbable². Resorbability is an often sought after characteristic of calcium phosphates so that they can be gradually replaced by newly formed bone. The objective of this study was to prepare a resorbable surface microstructured tricalcium phosphate (TCP) ceramic and evaluate its osteoinductive property and resorption rate after intramuscular implantation in dogs. This material was then compared to the established and slowly resorbable osteoinductive biphasic calcium phosphate ceramic (BCP).

Materials and Methods

Calcium phosphate ceramics: Calcium phosphate powders with the Ca/P ratios of 1.61 (BCP) and 1.50 (TCP) were mixed with diluted H₂O₂ solution and naphthalene particles to produce slurries. After foaming, drying and evaporation of the naphthalene, the materials were sintered for 8 hrs at 1150°C (BCP) or 1100°C (TCP). After milling, ceramic particles with a size of 1 to 3mm were sieved, cleaned and steam sterilized.

Chemistry and microstructures: The materials of interest were evaluated by XRD, and their microstructures were observed with SEM.

Calcium release: 0.5 ml ceramic particles (n=3 per material) were soaked in 100 simulated physiological solution (SPS) at pH 7.3 and 37±1°C for 200 minutes, the calcium concentration was measured continuously with a calcium electrode.

In vivo study: 1.0 ml ceramic particles (600±10mg per material per implant) were implanted in the paraspinal muscles of dogs (n=21). The animals were sacrificed after 6 weeks (8 animals), 12 weeks (8 animals) and 52 weeks (5 animals) respectively.

Histology and histomorphometry: The samples harvested were fixed, dehydrated and embedded in MMA. Non-decalcified sections were made cross the middle for histological observation. The area percentage of bone and materials was measured by histomorphometrical analysis. Paired t-test was performed to evaluate the difference and p<0.05 was set as the significant difference.

Results

BCP was composed of 20±5% β-TCP and 80±5% HA by weight as shown in XRD analysis, while TCP was comprised of more than 90% β-TCP phase. Similar microstructures (grain size and micropores) were observed under SEM for the BCP and TCP ceramics. TCP showed a higher calcium release than BCP in SPS7.3.

Table 1. A summary of bone and materials in implants at different time points.

		6wks	12wks	52wks
BCP	Bone incidence	7/8	8/8	5/5
	Bone%	1±1	11±6	15±5
	BCP	53±4	44±8	43±4
TCP	Bone incidence	2/8	8/8	5/5
	Bone%	0.02±0.02	15±10	26±6
	TCP%	53±4	33±4	13±3

The tissue responses to BCP and TCP ceramic particles, with regard to bone formation and material resorption are summarized in Table 1 and illustrated in Figure 2,

right. For both TCP and BCP, the area percentage of bone increased from 6 weeks to 12 weeks (p<0.05), while there was no significant increase after 12 weeks. Difference in bone formation between BCP and TCP was not seen although it should be mentioned that the absolute area percentage of bone was smaller in time for TCP due to degradation of this material.

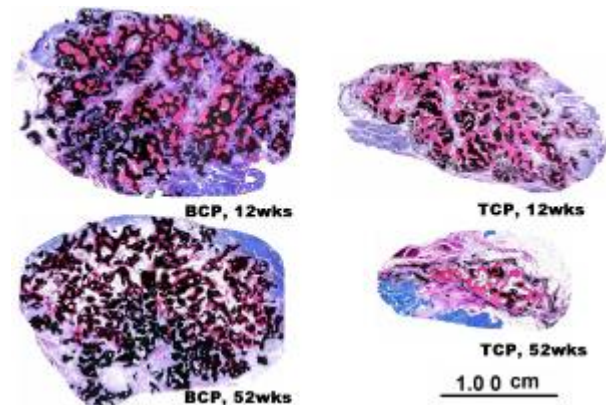


Figure 1. Histological overview of BCP and TCP implanted in muscle of dogs for 12 weeks and 52 weeks showing bone formation and resorption of TCP with time as compared to BCP.

Resorption of BCP was hardly seen either histologically (Figure 1) and histomorphometrically (Figure 2, right), while resorption of TCP from 6 weeks to 52 weeks was evident (p<0.05), as indicated by the decrease of implant size (Figure 1) and the signs of cell-mediated resorption (Figure 2, left). More than two third (2/3) TCP was resorbed after 52 weeks of implantation.

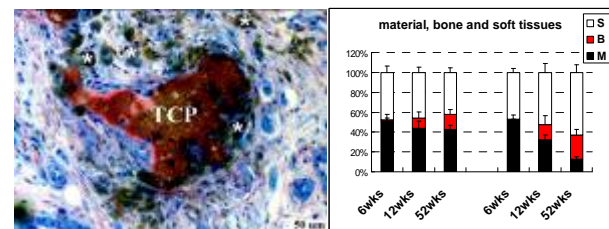


Figure 2. Left, cell-mediated resorption of TCP at week 12; right, percentage of bone, materials and soft tissues in BCP and TCP implants at different time periods.

Discussion and conclusion

We have successfully developed a surface microstructured, degradable tricalcium phosphate that has excellent osteoinductive properties. The osteoinductive potential was similar between TCP and BCP. Resorption of the TCP in time was demonstrated both histologically and histomorphometrically. Both chemical dissolution and cell-mediated resorption was observed resulting in almost 90% TCP loss after 1 year of implantation.

References

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