

# INTERNATIONAL JOURNAL of SPINE SURGERY

## A brief summary of 15 years of research on beta-tricalcium phosphates

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*Int J Spine Surg* 2009, 3 (3) 112-113

doi: <https://doi.org/10.1016/j.esas.2009.09.007>

<https://www.ijssurgery.com/content/3/3/112>

This information is current as of May 10, 2025.

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## A brief summary of 15 years of research on beta-tricalcium phosphates

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Porosity enhances cellular ingrowths and bone tissue formation but impairs the mechanical strength of calcium phosphate ceramics.<sup>1</sup> We have measured the compressive strength of hydroxyapatite (HA) ceramic with increasing porosity rates 20–60% and pore size 5–400 nm. After mathematical reconstruction of the data, the results showed that both the total porous volume and pore size of the ceramics influenced the mechanical strength, and that appropriate control of these characteristics allows for designing calcium phosphates implants with suitable mechanical strength and bone ingrowths capacities for bone grafting, even in load bearing applications.

In the early 90's, very little clinical data was available on  $\beta$ -tricalcium phosphates ( $\beta$ -TCP) ceramics as bone substitutes.<sup>2</sup> Considering 2 groups of patients, we have evaluated the quality of fusion with  $\beta$ -TCP (50% porosity) versus allograft (cortico-cancellous chips) in postero-lateral fusion from a consecutive series of 54 idiopathic scoliosis by

means of clinical and radiological evaluation over a period of up to 4 years. Tricalcium phosphates resorption was total after 2 years, while allograft fragments were visible on x-rays at the same delay. Loss of correction was 8% in the allograft group and 2% in the TCP group. Loss of correction did not progress after 6 months in the TCP group and after 2 years in the allograft group. These findings supported the clinical use of TCP ceramics in posterior lateral (PL) grafting and confirmed absorption of the material over time.

$\beta$ -TCP ceramics promote bone healing and are absorbed over time by surrounding cells and tissues.<sup>3</sup> What is the fate of the ions dissolved from the material in vivo? We have implanted nuclear radioactivated  $\beta$ -TCP ceramics (50% porosity) in the femoral condyle of rabbits for 1, 3, and 9 months and the implants were studied using histology, histomorphometry, and radio counting (autoradiography) techniques. Over time, the pores were invaded by connective then bone tissue (80%) and resorption of the implant (40%) was visible both at the outer surface and inside the pores. Bone formed inside the pores was radioactive and the radioactivity measured was consistent with the theoretical mineral content of woven bone formed in the early stages of endochondral ossification, suggesting that the ions dis-

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doi:10.1016/j.esas.2009.09.007

solved from the ceramic during the resorption process are re-used locally by osteoblast cells to synthesize the extracellular bone matrix. This finding supports the hypothesis that the fate of calcium and phosphate ions dissolved from  $\beta$ -TCP ceramics is similar to that of native bone minerals.

$\beta$ -TCP ceramics are efficient in general bone void filling in non load-bearing applications. Can such implants also be efficient in load-bearing conditions like anterior cervical disk fusion (ACDF)? We followed over a 3-year period a series of 33 patients who underwent ACDF [soft disc herniation (30%), calcified disc herniation (36%), trauma (30%), narrow cervical canal (4%)] and implanted with a  $\beta$ -TCP anatomical interbody cage (30% porosity; 90 MPa) and an anterior plate. Clinical [neck disability index, visual analog scale (VAS), neurological evaluation] and radiological (anteroposterior, lateral, bending x-rays) evaluation evidenced results similar to autograft or non-resorbable cages from literature data with no complication because of the implant. No nonunion was observed (dynamic x-rays). Resorption of the  $\beta$ -TCP cage was 50% approx. at latest follow-up, significantly less advanced than with more porous  $\beta$ -TCP in other indications. None of the implants had fractured. This study supported the hypothesis that  $\beta$ -TCP implants with suitable porosity and mechanical strength can efficiently replace the use of autograft, even in load-bearing applications.

$\beta$ -TCP ceramics can withstand high compressive stresses but have poor tensile strength and thus cannot be used under torsion or bending stress conditions.<sup>4</sup> We have developed a new  $\beta$ -TCP/poly-L-lactic acid (PLLA) composite material with improved young modulus and tensile strength. Pre-clinical biological evaluation of this material was carried-out in vitro and in vivo considering sample implants with increasing  $\beta$ -TCP content in the range [0–60%] w/w. In vitro evaluation [IL-1 $\alpha$  secreted by monocytes, cell proliferation (counting) and phenotypic expression (alkaline phosphatase [ALP] and I collagen) in human osteogenic cells] showed that adding increasing percentages of  $\beta$ -TCP to a lactic acid polymer matrix stimulated the proliferation of human osteogenous cells and synthesis of the extracellular bone matrix in a dose-dependent manner. In vivo evaluation in the rabbit (histology, histomorphometry) indicates that, in comparison with pure PLLA, tricalcium phosphate-containing composite materials had faster degradation kinetics, caused less inflammatory reaction, and promoted contact osteogenesis. The composite material containing 60%  $\beta$ -TCP demonstrated a similar performance to pure tricalcium phosphate grafts in terms of osteogenesis, and is compatible with the production of intra-osseous im-

plants for situations representing high levels of mechanical strain. Can this be clinically confirmed?

A cervical interbody fusion cage has been elaborated from a resorbable composite material with a high rate of  $\beta$ -TCP (60%  $\beta$ -TCP/40% PLLA).<sup>5</sup> We carried out a prospective study for evaluating the clinical and radiological results of 20 patients implanted with 27 composite cages (mean follow-up, 27 months). Clinical (neck disability index, VAS, neurological evaluation) and radiological (anteroposterior, lateral, bending x-rays) data were assessed before and after surgery. At the end of the study, computed tomography (CT) scan was performed to evaluate fusion, resorption of the cage, and density of the new tissue substituting the cage. The mean patient age was 50.3 years (range, 18–79). The average improvement was 55% for neck pain, 83% for arm pain, and 65% for neck disability index (NDI), with 85% good or excellent results at final outcomes. Radiologically, lordosis was improved significantly (mean gain of 5.4° and 3.7° for overall and segmental lordosis, respectively). This correction was conserved in 95% of cases. Fusion was obtained in 96% (CT evaluation). Resorption was started in all cases and completed in an average of 36 months after surgery. The mean density of tissue substituting the cage was 659 unit Hounsfield (UH) with a range of 455–911 UH (compatible with bone nature). Over time, the amount of bony tissue increased and the graft remodeled with an increase in density value. This demonstrates a biological activity and changing bone mineral content of this tissue. The new composite cage under investigation provides long-term fusion without loss of correction or inflammatory reaction.

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