Improved and more predictable vertical bone augmentation using synthetic dicalcium phosphate block grafts containing a novel bisphosphonate-EP4a conjugate drug (C3)

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BACKGROUND & OBJECTIVES
The long-term success of dental implants is dependent upon the degree of osseointegration in sufficient and healthy bone.1,2 Synthetic alternatives to replace autografts for alveolar ridge augmentation are actively sought to overcome autograft limitations such as extended operative time, the risk of infection and most importantly, limited quantities of autologous bone available.3-9 It has been shown that dicalcium phosphate (DCP) biomaterials, brushite and monetite are biocompatible, osteoconductive and resorb faster and more than other materials such as hydroxyapatite (HA).4 Brushite is stronger than monetite but resorbs less and converts to slowly resorbing hydroxyapatite after implantation.5-6 Whereas, Monetite resorbs faster and does not convert to HA resulting in greater bone infiltration.4,5 We have developed DCP grafts (monetite) that incorporate in their matrix a novel bone anabolic conjugate (C3) of an inactive bisphosphonate (bone targeting agent), an enzymatically hydrolysable linker and a potenti osteoblast activating agent (a potent and selective agonist for the EP4 prostaglandin receptor subtype) The primary objective of this research was to investigate whether the EP4a released from the conjugate drug C3 within the matrix of the monetite grafts has the potential to achieve rapid, enhanced and clinically significant bone regeneration in the vertical dimension in a proclival rabbit calvarial model.

METHODOLOGY
FABRICATION OF DCP GRAFTS WITH & WITHOUT C3 DRUG
*Brushite block grafts (9.5 mm x 4 mm) with and without C3 drug (0.1% concentration) in the matrix were fabricated using Beta-tricalcium phosphate (β-TCP), Monoclinic calcium phosphate monohydrate (MCPM) and deionized water (with and without C3 drug)
*The pre-set brushite block grafts were converted to monetite by autoclaving treatment. It was confirmed that this did not affect the C3 drug adversely.
*The Grafts were characterized for porosity (%), density (2.85 g/cm3) and mechanical strength. (6.5 MPa compressive strength)
IMPLANTATION & ANALYSIS OF THE GRAFTS
*The monetite grafts were implanted in pairs on 6 White New Zealand rabbit calvaria for 12 weeks stabilized with titanium screws (mm for each group)
*After 12 weeks, the animals were sacrificed and the grafts with calvarial bone blocks harvested and analyzed for bone augmentation and graft resorption using electron microscopy and histomorphometry. ** Mann-Whitney test was used to evaluate head-to-head differences between the implanted grafts and statistical significance value was set at a P < 0.05.

RESULTS

CONTROL & CLINICAL RELEVANCE
*The C3 containing monetite grafts integrated well onto the bone surface with mature bone extending through the graft area, while the C3 lacking grafts showed absence of mature bone and surface integration. In addition, the C3 containing monetite grafts demonstrate bone growth vertically up along the titanium screw surfaces which would be clinically very relevant in terms of implant stability and osseointegration.
* Some potential advantages of using these monetite/C3 graft materials are: Faster bone healing; Better quality bone (improved implant stabilization); Faster Implant Integration; Predictive regeneration of bone around teeth and implants and no need for donor site. Here we present results from a novel anabolic bone graft formulation and confirm its efficacy in an implantation model which promises to ultimately benefit millions of patients undergoing bone augmentation for dental implant therapy.

REFERENCES
5. FUNDED BY: CIHR POP Grant
American Academy of Implant Dentistry Foundation (AAID).
Alpha Omega Foundation of Canada.