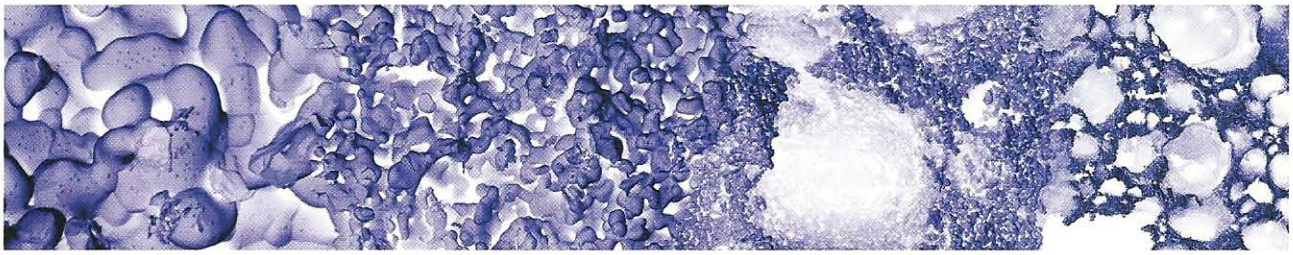
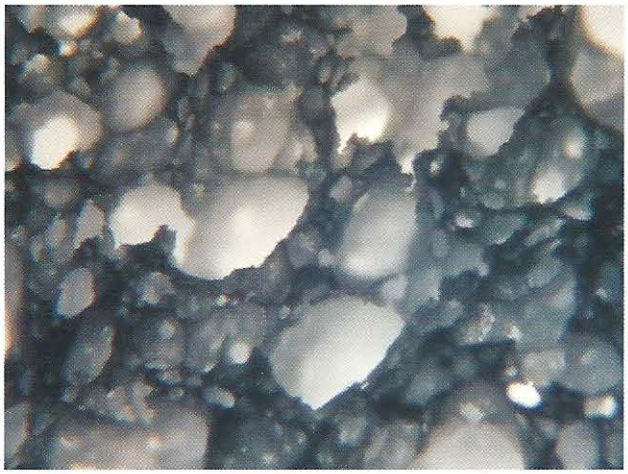
Orthogem

enhancing bone biology



TriPore™

the new generation advanced synthetic bone graft



TECHNICAL OVERVIEW

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Introduction

Synthetic Bone Grafts (*SBGs*) have been commercially available since the early 1960s. Back then it was believed that almost any calcium phosphate based product bearing a passing resemblance to cancellous bone would perform. It was soon realised that this was not the case and since then many variations of the same technology have been tried in the quest to find a product to compete with autograft, the accepted 'gold standard'.

Orthogem was founded on the observation that the manufacturing technologys for conventional SBG's produce a microstructure which, although similar in appearance to cancellous bone, simply do not produce the appropriate environment for bone regeneration. Orthogem's scientists concluded that until the basic microstructure was refined, very variable performance would result.

TriPore **from Orthogem** – *designed to enhance bone biology*

Orthogem's scientists designed TriPore from the bottom up by first considering what the optimal microstructure for osteogenic activity should be. Then, with this ideal structure in mind, they set about creating an entirely new manufacturing process to produce this structure. The results speak for themselves:

- Restores homogenous osteocyte density within the graft site

  Recruits and actively conducts osteogenic cells throughout the graft Micro-structural 'superconduction'
  Osteocyte manipulation stimulates natural bone formation

- Total resorbtion of the ceramic SBG

  No compromise in graft site strength or viability

- 'Fit and Forget'

Front page micrograph shows TriPore HA under back lit optical microscope. It is possible to see the macropores as well as the interconnecting midipores which provide the graft with its superconductivity.

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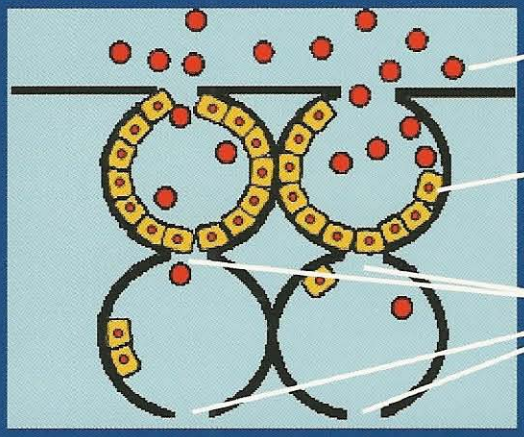
TriPore - different by design

A. Conventional SBG microstructure



Osteoprogenitor cells

Osteoblasts

Connecting pathways easily blocked reducing conductivity

Relatively few interconnecting pores

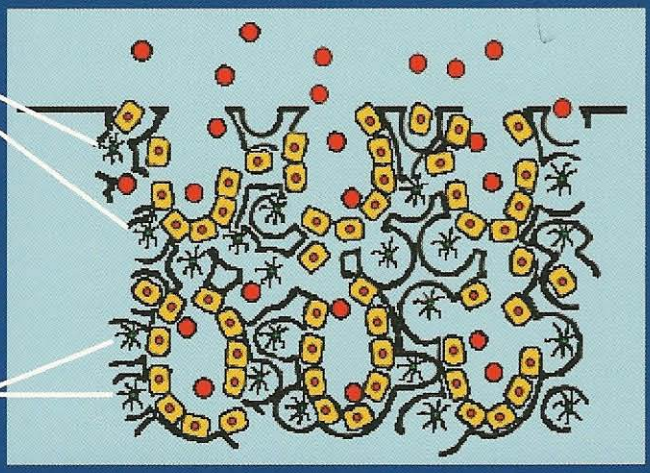
Bone may struggle to grow into 'conventional' SBG microstructures, since its pores are easily blocked. This is a simple physical phenomenon and totally unrelated to chemical composition or bioactivity. Chemically modifying the structure to enhance bone formation does not take into account this microstructural deficiency.

B. ***Tri****Pore's advanced microstructure*

Midipores within the connecting walls allow osteocytes to populate the whole implant body at a very early stage

Large numbers of pores prevent blocking of the microstructure

Midipores mimic natural lacunae in mediating osteocyte formation



TriPore encourages osteocytes formation throughout the entire ceramic body, not just at the graft surface.

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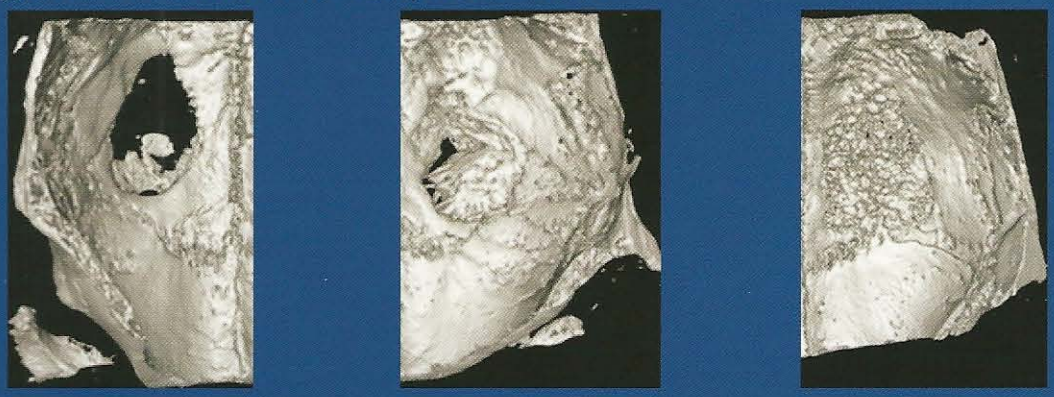
Design validated through extensive preclinical evaluation

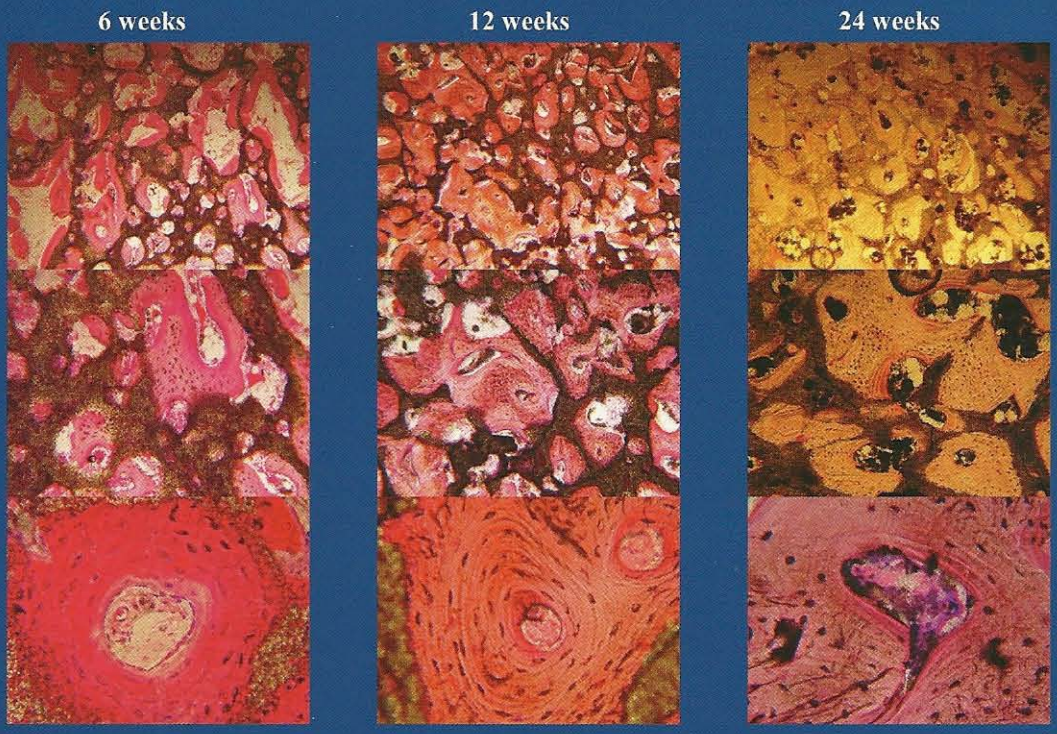
Before embarking on clinical evaluations, Orthogem put TriPore through a rigorous and extensive programme of scientific testing and validation[1].

Studies were carried out using a variety of animal models and resulted in full validation of the design hypothesis behind the advanced porous structure.



A B C

CT images of TriPore granules at 6 weeks post implantation in a critical size defect in a rabbit cranial model. The control group had defects in one side left unfilled (A), whilst the other side was filled with autogenous particulate bone harvested from the cranium (B). A second group had defects in one side filled with TriPore granules (C).



Histology of TriPore HA in sheep femoral condyle model at 6, 12 and 24 weeks shows the development of high quality bone and the formation of new blood vessels within the graft. Infiltation of bone into the remaining graft materials demonstrated TriPore's continuing ability to remodel into high quality bone.

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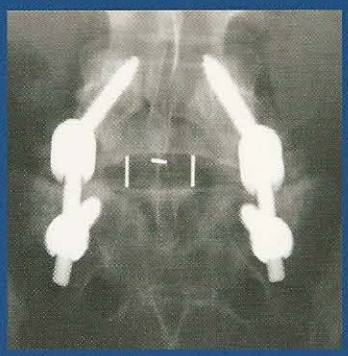
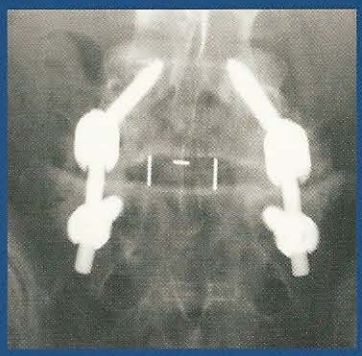
Clinical evaluation of TriPore

TriPore has been successfully validated in a number of spinal indications where it has reinforced the performance demonstrated in pre-clinical studies.

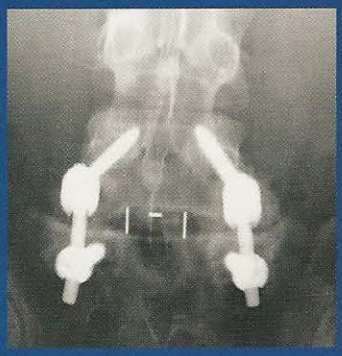
Case 1 Transforaminal Lumbar Interbody Fusion at L5/S1 in 38 years old male.



3 months post-op

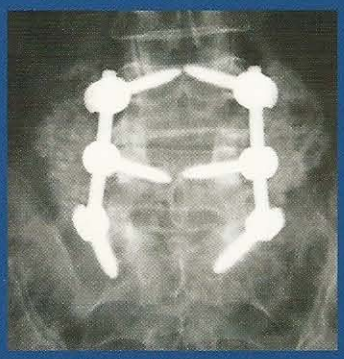


6 months post-op

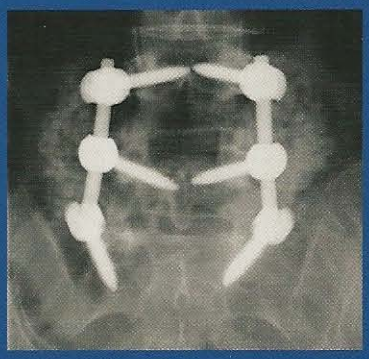


12 months post-op

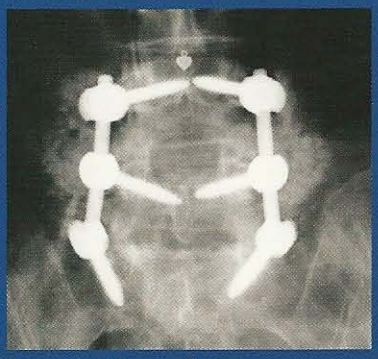
Case 2 Postero-Lateral Spinal Fusion at L4/S1 in 62 years old female.



3 months post-op



6 months post-op



12 months post-op

Both cases have solid fusion with continuous columns of new bone demonstrate the effectiveness of TriPore's structure, validating the assertion that TriPore is the 'fit and forgot' advanced synthetic bone graft.

Advantages of TriPore Synthetic Bone Graft

- **Superior porous structural design confirmed through extensive pre-clinical testing[1]**
- **Supercconduction guides bone growth throughout the whole implant site**
- **Resorbed at the same rate as new bone formation, resulting in a strong and viable graft site**
- **Fully resorbed, even in HA form**
- **Excellent clinical results [2]**
- **Reliable and consistent performance**
- **Available in various block and granule sizes to meet clinical need**
- **Part of an extensive R&D program of advanced synthetic bone solutions**

1. *Orthogem TriPore: A new resorbable hydroxyapatite bone graft substitute: proof of biological concept in a long term sheep femoral condyle model. Birch N, Lo W, Frohn M, Blunn G, Goodship A.*
2. *'Results of TriPore Synthetic Bone Graft' Clinical 'White Paper'. Data on file at Orthogem Limited.*

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For further information concerning **Tri**Pore, please contact your local sales specialist.

www.orthogem.com