INTRODUCTION
Bony defect treatment is challenging due to the associated morbidity using autograft, potential disease transmission or limited availability using allograft and the plethora of bone graft substitute materials available. Chemistry, size, shape and porosity of substitute materials can all potentially influence the in vivo response. This study evaluated the influence of the porosity of particulate calcium phosphate bone graft substitutes in a bilateral tibial defect model in New Zealand (NZ) white rabbits based on radiographic, mechanical, histomorphometry and histology.

METHODS
A bilateral defect model [1] (5 mm wide and 15 mm long) spanning the metaphyseal and diaphyseal region was created 3 mm below the joint line in the anteromedial cortex of the proximal tibia in 40 skeletally mature NZ white rabbits following ethical approval. Defects were created using a microburr with a 3 mm diameter tip under saline irrigation. The defects were flushed with sterile saline prior to being filled with 4 different calcium phosphate bone graft substitutes (table 1) to the height of the original cortex. Samples were x-rayed in the A-P and M-L planes using high resolution mammography film. Tibias were embedded in Wood’s metal and torsion tested to failure. The tibias were then embedded in PMMA, sectioned and examined using back scattered SEM for histomorphometric analysis of bone, implant and void (n=8 per group per time point) [1]. Two samples per group per time point were processed for routine paraffin histology. Time Zero samples were examined with radiographs and SEM only. Histomorphometry and mechanical data was analysed with a 2-way analysis of variance. Radiographs and histology were qualitatively assessed in a blinded fashion for implant resorption and in vivo response.

RESULTS
X-rays of the raw materials revealed marked differences in the appearance and porosity between the 4 materials (image below). X-rays taken over time revealed a progression in new bone formation and healing of the defect while little was noted for implant resorption. New bone formation was observed by 4 weeks (all groups) and evidence of resorption at 12 weeks for Actifuse. All defects appeared well healed by 12 weeks with new bone formation in concert with the implanted materials.

During torsion testing all samples failed in a spiral fashion initiated at the distal margin of the defect. The mechanical properties increased as the defects healed and new bone formed over time. No differences were noted between materials. SEM revealed a progression of new bone formation with time for all materials. New bone ingrowth into the porous domains and ongrowth to the surface of the materials was evident at 2 weeks and progressed with time. The synthetic HA materials did not show any resorption based on histomorphometry versus time. OsSatura (HA/TCP) revealed a 40% loss of implant by 12 weeks compared to time 0 (p<0.05). For comparison, a HA/calcium carbonate bone graft (ProOsteon 200R, Interpore-Cross) at 12 weeks [1] is presented in the graph (below) using the exact same model and experimental conditions. New bone ingrowth was superior to 200R (p<0.05) in all 4 materials (current study) at 12 weeks. Implant resorption was greater for 200R compared to these materials at 12 weeks (p<0.05).

DISCUSSION
A bilateral metaphyseal - diaphyseal tibial defect in adult rabbits was used to examine implant resorption and bony response of 4 bone graft substitutes in particulate form (table 1) at 2, 4, and 12 weeks. The metaphyseal defect of width 5 mm and 15 mm in length represents a large defect in the anteromedial rabbit tibia. The empty defects do not heal in this model, supporting the critical nature of this defect [1]. New bone formed at the margins of the defect, posterior endosteal cortex and within the defect itself, confirming the osteoconductive nature of the materials examined. The performance of all 4 materials was similar in this model while they were all superior to ProOsteon 200R based data using the identical experimental conditions [1].

The macroscopic, microscopic and chemical differences in the materials did not result in any major differences in in-vivo bone response in terms of mechanical properties or histomorphometry data apart from implant resorption (as expected for the HA/TCP material). The lack of any differences may reflect the use of these materials in particulate form as opposed to solid blocks. Hing et al., [2] recently reported that microroporosity enhances bioactivity of synthetic bone graft substitutes. The packing of the defect, voids, and placement of the material may override the differences in material microporosity when in particulate form. No advantages were observed when the materials were reduced to particles and placed into the defect. Differences in particle size may also account for differences in percent void in the defects. Interestingly, the OsSatura material is reported to have particle size of 1-5 mm whilst the other materials studied were 2-5 mm in size. This difference in particle size may influence the overall void in the defect and packing as well as available surface area. The slow degradation profile of the synthetic materials may also contribute to an overall slower new bone formation due to the presence of the material itself. These materials do demonstrate overall excellent biocompatibility and osteoconductive properties.

REFERENCES

AFFILIATED INSTITUTIONS
* ApaTech Ltd, Queen Mary, University of London, London, E1 4NS

Table 1: Study design

<table>
<thead>
<tr>
<th>Implant</th>
<th>Material</th>
<th>Porosity</th>
<th>Particle size</th>
<th>Time points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apapore-60</td>
<td>Synthetic HA</td>
<td>60%</td>
<td>2-5 mm</td>
<td>2, 4, 12 wks</td>
</tr>
<tr>
<td>Actifuse</td>
<td>HA, 0.8% Silicon substituted</td>
<td>80%</td>
<td>2-5 mm</td>
<td>2, 4, 12 wks</td>
</tr>
<tr>
<td>Apapore-80</td>
<td>Synthetic HA</td>
<td>80%</td>
<td>2-5 mm</td>
<td>2, 4, 12 wks</td>
</tr>
<tr>
<td>OsSatura</td>
<td>80% HA, 20% β-TCP</td>
<td>75%</td>
<td>1-2 mm</td>
<td>2, 4, 12 wks</td>
</tr>
</tbody>
</table>

52nd Annual Meeting of the Orthopaedic Research Society
Paper No: 1716