USE OF OP-1 IN FEMORAL IMPACtION GRAFTING IN A SHEEP HEMIARTHROPLASTY MODEL

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Introduction
At revision total hip replacement, impaction allografting of the femur is used to restore bone and enhance stem fixation. While good results have been reported, the results of this procedure have been variable, with prosthesis subsidence and fracture being reported in some cases1 and incomplete bone incorporation and remodelling reported in human retrievals even at long term2. Biological manipulation of allograft, including the use of bone morphogenic proteins (BMP) might theoretically enhance bone graft incorporation and possibly improve results. BMP-7 (OP-1) has been shown previously to promote neovascularisation of the graft and new bone incorporation and remodelling of the stem in a segmental defect model3, however its use in a loaded impacted bone graft situation has yet to be established. Therefore, a study was undertaken using a sheep model of cemented hip hemiarthroplasty with femoral impaction grafting. The aims were to examine bone graft incorporation during the first 6 months, to compare graft incorporation in femurs impacted with allograft bone or with allograft bone augmented with 2.5mg OP-1 in a type I collagen carrier, and to determine if there are any adverse affects of OP-1, including excessive bone resorption or inflammatory cell activity, given that osteoclast induction and proresorptive activities have been seen with BMPs4-7.

Methods
Twelve sheep underwent a left hip hemiarthroplasty with a cemented polished tapered stem and impaction of morsellised allograft bone alone in six sheep (control group) or with morsellised allograft bone and OP-1 in six sheep (OP-1 group). The sheep were allocated into groups of four which were sacrificed at 6, 18, and 26 weeks. There was one traumatic femoral fracture requiring early sacrifice and replacement with another sheep so that there were two control and two OP-1 sheep sacrificed at each time period. The study was approved by the institutional Animal Ethics Committee. Outcome measures included clinical performance, manual measurement of stem subsidence from plain radiographs, histological evidence of bone graft incorporation and remodelling, and fluorochrome bone labelling to determine bone apposition rates. The extent of graft incorporation with new bone, and remodelling in the grafted regions was scored using the system described by Salkeld et al (2001)7 modified for this model and to include grades for adverse tissue response.

Results
Clinical findings: One sheep in the 18 wks control group and one sheep in the 26 wks OP-1 group were slow to fully weight-bear postoperatively but had good gait for the remainder of the study period. One sheep in the 26 wks control group developed a limp at 23 wks postoperatively that persisted until sacrifice. The remaining sheep in the control and OP-1 groups demonstrated good gait.

Histological findings: In the 6wks control group there was invasion of the allograft by fibrovascular tissue, usually partial resorption of the graft and deposition of new bone onto all or part of the remaining graft (Figure 1). In the OP-1 group at six weeks, there was neovascularisation of the graft with resorption of usually most of the graft. The graft was replaced by new bone within dense fibrovascular tissue (Figures 2). In areas of bone formation in the proximal femur, the percent of bone that was new host bone ranged from 88-100% in the OP-1 group and 6-88% in the control group. In both groups, graft incorporation decreased proximally to distally and from the endocortex to the cement interface. Fluorochrome bone analysis confirmed that bone formation activity was the greatest in the proximal sections and decreased in the mid and distal sections at six wks. The bone apposition rate, measured at between 5 and 6 weeks postoperatively ranged from 0.9 to 2.9µm of new bone per day. At six wks, in the tissue in the grafted regions of the femurs, there were no differences between the groups in the mean percent of labelled bone or the bone apposition rates. At six wks, in the cortical and ungrafted trabecular regions of the femurs, the mean percent labelled bone was higher in the OP1 group than in the control group. At 18 wks there was new bone formation and active remodelling and trabeculation of the new bone at each level of the stem in the OP-1 group. This was less in the control group, particularly at the level of the mid and distal stem where unincorporated bone was seen. In both groups, at 26 wks there was remodelling of bone in the original grafted region. In the OP-1 group there had been extensive remodelling of the new trabecular bone resulting in a decreased density of the trabecular bone and large areas of mature fatty marrow present adjacent to the cement (Figure 3), particularly at the level of the mid and distal stem. The amount of original allograft bone was greater in the control femurs. Infiltrates of lymphocytes were occasionally seen in the grafted region in both groups. Small regions of fibrous tissue were occasionally seen at the cement-bone interface in both groups.

Scoring of the histology showed that bone graft incorporation and remodelling progressed over the 26wks and the biggest difference in graft appearance between the control and OP-1 groups was at 6wks (Figure 4).

Discussion
This longitudinal study showed that over a 26 week period there was incorporation and subsequent remodelling of control allograft and OPI treated allograft in femurs undergoing cemented hip hemiarthroplasty in sheep. Importantly, the results suggest that OP-1 may hasten graft incorporation and remodelling, and this is the first evidence of this in an animal model that is similar to the human situation. In this preliminary time course study, the numbers of study animals was too small to exclude major adverse effect of augmenting morsellised allograft bone with OP-1 in femoral impaction grafting. However, the results thus far are encouraging, there being only two major problems, one significant subsidence in the OP-1 treated group and one case of possible radiographic loosening in the control group. The potential benefits and possible risks of the use of BMPs and allograft in this way require further investigation with larger numbers examined at selected time points, and this study provides important data for planning such studies.

References:

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Radiographic findings: Stem-cement subsidence ranged from −1.1 to 7.5mm. Neither the treatment nor the implantation time influenced the degree of stem-cement subsidence. The median subsidence at the cement-bone interface was 0.7mm with only one stem subsiding more than 3.5mm. There was no difference between the groups, but the numbers of sheep are small. A cement-bone interface radiolucency of between 50-99% was seen in one 18 wks control femur.

Figure 1. New bone incorporating original graft particles (arrows) (6wks control gp. tol blue, 100x Mag)

Figure 2. New bone (b) in grafted region continuous with trabecular bone (6wks OP-1 gp. tol blue, 40x Mag)

Figure 3: Trabecular bone within a fatty marrow in the original grafted region (26 wks OP-1 gp. tol blue, 40x Mag)

Figure 4. Histological scoring of bone graft incorporation and remodelling

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