Introduction. Large segmental long bone defects above critical-size do not heal. Ideally, bone graft substitutes having optimal biological and structural properties might be used to promote new bone formation. As such ideal substitutes are not available, autogenic cancellous bone graft is commonly used to heal large bone defects irrespective of the drawbacks of the graft harvesting procedure. Healing of unicortical defects in the iliac crest with preserved cortex may take up to 2 years. Tricortical defects do not heal. Hence, there is still a need for new more effective cancellous bone graft substitutes. Such substitutes could be used instead of autogenic bone graft as self-standing implants, and/or be applied to enhance and accelerate healing of the iliac crest defects. It has been previously reported that unicortical defects in the iliac crest of healthy sheep not covered with cortex but implanted with biodegradable polyurethane cancellous bone graft substitutes were healed with new dense cancellous bone within 4 to 6 months.

This study addressed the question of whether it was possible to heal defects in the iliac crest of estrogen-deficient sheep by implanting experimental porous biodegradable polyurethane cancellous bone graft substitutes and whether their chemical composition and porous structure affects the healing process.

Materials and Methods. Bone substitutes: Porous plugs 10 x 10 mm were produced from experimental elastomeric biodegradable polyurethanes having the hydrophilic-to-hydrophobic unit ratio of 30-70%, 50-50% and 70-30%, respectively. The hydrophilic segment was based on poly(ethylene oxide) diol and the hydrophobic segment on poly(ε-caprolactone) diol. In addition, the calcium complexing moiety, the polysaccharide and/or vitamin D3 were incorporated in the polymer. Implants were sterilized by a cold-cycle ETO process and subsequently evacuated under a high vacuum. Animal model: Twenty one skeletally mature (> 4 years; 38-49 kg) Warhill ewes ovariectomized 12 months prior to implantation of the porous polyurethane plugs were used in the experiments. Surgery: Under general anaesthesia 10 mm (diameter) x 10 mm (length) holes were drilled through both cortices of the tuber coxae and implanted (press-fit) with elastomeric polyurethane plugs soaked in Ringer solution (IACUC protocol # 99-228A-02). Similar defects not implanted with polyurethane plugs were used as control. Subcutaneous wounds were closed in layers using 2/0 braided lactomer (Polysorb) sutures and the skin was closed with stainless steel staples. Tetracycline (LA-200; Pfizer) was injected twice prior to sacrifice (1:11:1:3-5 protocol) at a dose of 25 mg/kg. The animals were humanely euthanized 18 and 25 months after implantation using barbituric acid overdose. The control and implanted iliac crest bone were harvested. Macroradiographic images were taken from histological sections of the explanted, operated ilium. The sections were stained with giemsa/eosin for histological evaluation.

Results. The porous polyurethane implants had the average pore size in the range of 300 to 2000 µm. The pore-to-volume ratios of the scaffolds were in the range of 85% to 89% (Fig. 1).

Fig. 1. Scanning electron micrograph of polyurethane implants with various chemical compositions. A. 70-30 phil-phob+vitamin D3; B. 50-50 phil-phob+polysaccharide; C. 70-30 phil-phob+Ca-complexing additive; D. 30-70 phil-phob+ Ca-complexing additive. All animals survived the planned implantation period of 18 - 25 months. At this time the defects in the iliac crest were healed with new bone (Fig. 2). The extents of bone healing were depended on the polymer chemical compositions, although for the same material there were animal related differences in healing. The polymers with incorporated calcium-complexing additive were more effective, followed by those with vitamin D3 and polysaccharide-containing polymer. Newly grown cancellous bone was radiographically similar to the native bone. No bone was found in the control defects. These were filled with fibrous tissue.

Discussion. Harvesting of bone graft from the iliac crest is traumatic and results in morbidity of the donor site. Any treatment modality, which could avoid the use of bone graft, would be beneficial. If, however, bone graft is to be used, then the enhancement of bone regeneration in donor site allowing for reharvesting should be the primary objective. This was achieved in the present study by using elastomeric cancellous bone graft substitutes from biodegradable polyurethanes. The healing process of defects in the iliac crest of estrogen-deficient sheep was comparable to that of the healthy sheep. It is worth noting that the structure of the cancellous bone formed in the iliac defects of healthy sheep was much denser than the native cancellous bone. The new cancellous bone forming in the iliac defects of estrogen-deficient sheep resembled the structure of the native bone.

Conclusions: Biodegradable, elastomeric porous polyurethane bone substitutes implanted in the iliac crest defects of estrogen-deficient sheep induced bone regeneration. Such implants could potentially diminish the morbidity of the donor site and allow for earlier reharvesting. Further short-term studies not exceeding 6 to 8 months are required to select the cancellous bone graft substitutes with optimal properties.