Introduction: Experimentally, growth factors such as BMP-2 have proven to promote spine fusion and to overcome the disadvantages of an autologous bone graft. The optimum method to deliver growth factors as well as the optimum growth factor to promote spinal fusion is still a matter of discussion. The purpose of this study was (1) to evaluate the effect of a biodegradable poly(D,L)-lactide (PDLLA) carrier system and (2) to evaluate the efficacy of transforming growth factor-ß (TGF-ß) and insulin-like growth factor-I (IGF-I) application by a poly-(D,L)-lactide (PDLLA) coated cage in a in vivo sheep cervical spine interbody fusion model.

Method: 32 adult female merino sheep (2 years old, average weight 57.2 +/- 3.5 kg) underwent C3/4 discectomy and fusion: The sheep were randomly assigned to the following groups: Group 1: autologous iliac bone graft (n = 8); Group 2: meshed titanium cage (n = 8); Group 3: meshed titanium cage coated with a biodegradable poly(D,L)-lactide (PDLLA) carrier (n = 8). Group 4: meshed titanium cage coated with a biodegradable poly(D,L)-lactide (PDLLA) carrier including TGF-ß (1% w/w) and IGF-I (5% w/w).

Surgical technique and postoperative care: All sheep underwent the surgical procedure under general endotracheal anesthesia. Via a left anterolateral approach discectomy C3/4 was performed. For fixation either a iliac crest bone graft of 8 mm height or a meshed titanium cage (Fa. Acromed-Depuy, height 8 mm, diameter 14 mm) were used. After surgery the animals received analgesia for 5 days intramuscularly. They were allowed ad libitum activity for the remainder of the experiment.

Radiographic analysis: Digital radiographic scans were performed pre- and postoperatively and after 1, 2, 4, 8, 12 weeks. At the same time periods, intervertebral disc space height (DSH), intervertebral angle (IVA) and lordosis angle (LA) were measured. After 12 weeks fusion sites were evaluated using digital functional radiographic views in flexion and extension and quantitative computed tomographic scans (QCT) to asses bone mineral density (BMD), bone mineral content (BMC) and callus volume (CV).

Biomechanical analysis: Biomechanical testing was performed by a non-destructive flexibility method using a nonconstrained testing apparatus. Pure bending moments were applied using a system of cables and pulleys to induce flexion, extension, left and right lateral bending and left and right axial rotation. Tension was applied to the cables with an uniaxial testing machine (Zwick 1456, Zwick GmbH, Ulm, Germany). Three-dimensional displacement of each motion segment was measured using an optical measurement system (Qualysys Inc., Sävebalden, Sweden). Non-linear diodes (Qualysys Inc., Sävebalden, Sweden) were attached to the bodies of C3 and C4. Marker positions were detected with two cameras and recorded with a computerized motion analysis system (PC-Reflex, Qualysys Inc., Sävebalden, Sweden). Angular displacement of the upper vertebra in relation to the lower vertebra was calculated from marker position using custom-made computer software. The experimental error associated with this method was +/- 0.1 degrees. The mean apparent stiffness values were calculated from the corresponding load-displacement curves. Range of motion (ROM), neutral (NZ) and elastic (EZ) zones were determined.

Statistical analysis: Comparison of data was performed using Mann-Whitney-U Wilcoxon rank sum test.

Results: Over a 12 week period the cage groups (group 2-4) showed significantly higher values for IVA (p< 0.05) and LA (p<0.05) compared to the autologous iliac crest graft group (group 1). Radiographic analysis of the radiographs revealed significant lower residual flexion/extension movement in the PDLLA coated cages with TGF-ß and IGF-I than in any other group (p<0.05). After 12 weeks BMD, BMC and CV were constantly higher in the PDLLA coated than in the non-coated cage, but there was no significant difference. The PDLLA coated cages with TGF-ß and IGF-I showed significant higher values for BMD (p<0.05), BMC (p<0.05) and CV (p<0.05) than in any other group (fig. 1). Average stiffness in rotation was significantly higher (p<0.05) and ROM, NZ and EZ in rotation were significantly lower (p<0.05) in the PDLLA coated cages with TGF-ß and IGF-I than in any other group. There was no significant difference for stiffness, ROM, NZ and EZ between the coated and the non-coated cages.

Conclusion:
(1) PDLLA-coating of cervical spine interbody fusion cages as a delivery system for growth factors showed no adverse radiographic and biomechanical effects on cervical spine interbody fusion. The positive effect of the PDLLA-coating on BMD, BMC and CV might be a result of degradation process of the biodegradable carrier.

(2) In comparison to the iliac crest graft, TGF-ß and IGF-I application by a PDLLA coated interbody cage significantly increased radiographic and biomechanical results of interbody fusion in the sheep cervical spine, while the donorside morbidity was excluded. TGF-ß and IGF-I coupled with a biodegradable carrier system clearly enhanced sheep cervical spine fusion velocity. Further in vivo studies of different growth factors are necessary to determine the “ideal” growth factor or growth factor combination for spine fusion.