INTRODUCTION:
It is well recognized that osteogenesis and differentiation of precursor cells is sensitive to the local mechanical environment. Several mechano-regulation algorithms have been proposed where different parameters are suggested to predict the tissue differentiation. However, corroboration of these algorithms has been difficult. This is partially because repeatable experimental outcomes under controlled mechanical environment are necessary, but sparsely available. In distraction osteogenesis (DO), a controlled displacement is applied to regenerate large volumes of new bone with very predictable outcomes. The aim of our study was to compare the results of the study of mechanical effects on bone regeneration. In a recent study, it was demonstrated that a mechano-regulation algorithm based on deviatoric strain and fluid flow was most consistent with experimental bone healing under both shear and compressive deformations. In this study, we hypothesized that this mechano-regulation algorithm would also be corroborated by the spatial and temporal tissue distributions seen experimentally during DO.

METHODS:
An ovine experimental study for evaluation of bone segment transport, which was conducted previously in our institution, was used for comparison. That study involved tibia shaft defects of 20 and 45 mm. After corticotomy, these were closed by transport of a segment over an unreamed interlocking nail (Fig. 1). Distraction started on post-operative day 1 with a rate of 1 mm/day until the defect was closed. During distraction, force and force relaxation were measured. Weekly standardized radiographs and undecalcified histology at the time of completion were available for comparison.

A mechano-regulated adaptive 2D axisymmetric finite element (FE) model (ABAQUS) of an ovine tibia with geometry resembling the experimental model (1 mm/24 hours), for 20 or 45 mm, was used for re-meshing. The model of DO was chosen due to its well-defined mechanical conditions, as well as final bony bridging. The distraction phase reached a steady state situation and similar tissue distributions were observed for 20 and 45 mm distraction.

RESULTS:
The predicted computational model data corresponded well to the experimental model data. The reaction forces calculated computationally, both after distraction and relaxation, agreed well with those measured experimentally. Initially, the maximal force experimentally was 30-60 N compared to 56 N predicted computationally. The corresponding force relaxation decreased exponentially with 60-70% after 24 hours compared to 67% computationally. The predicted tissue in the distraction gap was mainly fibrous during the first week. The bone formation was observed close to the periosteum and endosteum after 6 days. This was followed by bone formation within the gap area, which grew and became longer as distraction proceeded (Fig. 1cd). There was a steady gap with soft tissue in between the distraction ends of about 5 mm. Some periosteal callus was predicted. The predicted bone remained immature until distraction was finalized. During consolidation, maturation followed as well as final bony bridging. The distraction phase reached a steady state situation and similar tissue distributions were observed for 20 and 45 mm distraction.

DISCUSSION:
A mechano-regulation algorithm based on deviatoric strain and fluid flow was able to predict the bone formation pattern observed during DO from initial corticotomy to final consolidation. Furthermore, predicted distraction force and its daily relaxation agreed overall well with that observed experimentally. Comparison of soft tissue composition is still pending. The model of DO was chosen due to its well-defined mechanical conditions, as well as other bone forming processes. Now it has taken one step further towards corroboration by successfully predicting the bone formation pattern during DO. Furthermore, as relative amounts of endochondral vs. intramembranous bone formation during DO appear to be directly related to the distraction rate, and the local strain/stress generated in the distraction gap, such relationships may now be investigated with this algorithm to optimize and accelerate DO treatment protocols.