Introduction: Bone healing is a highly complex well-orchestrated regenerative process that leads to restoration of injured skeletal tissue to a state of normal structure and function. Although physiological bone repair is a rapid and efficient process, delayed union and non-union are still a severe complication during fracture healing, affecting up to 10-20% of patients. For the development of new effective therapies for patients, it is mandatory to get a more in-depth understanding of the patho-physiological processes during healing leading to delayed/non-union.

The aim of this study was to mechanically produce a standardized model for an experimental hypertrophic non-union in sheep for investigations of the patho-physiological healing processes occurring in fracture repair leading to non-union.

Materials and Methods: A mid-shaft osteotomy of the tibia was performed in two groups of sheep and stabilized with either a rigid (group I) or mechanically critical (group II) external fixator. The sheep were sacrificed at 6 and 9 weeks post-operatively (n=8, each). To demonstrate that the critical fixation leads to formation of a pseudarthrosis rather than just delayed healing, one further group treated with the critical fixator was sacrificed 6 months after surgery (n=8). The study was approved by the local legal representative (LAGeSo, Berlin: G0172/04).

Beginning 3 days postoperatively and then at weekly intervals, threedimensional interfragmentary movements were measured in the 9-week groups. Measurements of ground reaction forces were performed preoperatively and concurrently to those of interfragmentary movement. Following sacrifice, standardized cranio-caudal radiographs of the affected limb were taken and biomechanical testing of the healed and contralateral tibia was performed.

Statistical comparisons between the groups were performed using the Mann-Whitney-U test (SPSS 14.0) and the Bonferroni-Holm test procedure. A p-value of less than 0.05 was taken as a significant difference.

Results: Broad inter-individual variations could be observed for the analyzed interfragmentary movements and for the ground reaction forces preoperatively as well as postoperatively. Seven days postoperatively, the interfragmentary movements at the fracture site in group I amounted to 1.1° (range 0.8-1.9°) axial torsional movement, 0.7 mm (range 0.4-1.2 mm) shear movement in the cranial-caudal direction and 0.4 mm (range 0.2-0.6 mm) axial compression. In group II, interfragmentary movements of 11.6° (range 8.1-12.5°) axial torsion, and 9.5 mm (range 7.2-11.6 mm) shear and 2.5 mm (1.4-3.5 mm) axial compression were recorded at this time point. Whilst interfragmentary movements in group I showed only small changes over the course of healing, the movements in group II considerably decreased until the fourth week followed by an almost constant magnitude. At all investigated time points except for 42 days postoperatively, group II showed significantly higher interfragmentary movements in comparison to group I (p<0.048).

In both groups, the sheep unloaded the operated hindlimb. Maximum unloading in group I was reached in the second postoperative week. The maximum ground reaction forces in this group returned to their preoperative values within the observed 9-week period. In group II, the maximum unloading was more pronounced, took place 3 days after surgery and there was no return to the preoperative values.

Radiographic inspection revealed four bone-bridged cortices from 6 weeks onwards in all animals stabilized with the rigid fixator (group I). At 6 and 9 weeks post surgery, all animals belonging to the critical fixator group (group II) showed periosteal callus formation, but only partially bony bridging was achieved in 4 out of 8 animals and the osteotomy gap remained clearly visible. At 6 months postoperatively, 3 out of 8 animals in group II showed a non-union with much periosteal callus formation, at least on one cortical side. In the other 5 animals, complete bridging was achieved with almost invisible gap.

The torsional strength and stiffness of the tibiae stabilized with the critical fixator were higher than that of those tibiae stabilized with the critical fixator at 6 and at 9 weeks. At both time points, only 4 out of 8 tibiae stabilized with the critical fixator could be tested biomechanically, but there was no increase in either torsional strength or stiffness from 6 to 9 weeks. The rest of the specimens had negligible mechanical properties and were therefore not tested. At 6 months, 5 out of 8 tibiae of group II were tested, but 2 specimens had to be excluded from the analysis. The 3 tested specimens showed a considerable increase in torsional strength and stiffness from 9 weeks to 6 months (Fig. 1).

Discussion: This study describes the mechanical induction of a delayed osteotomy healing in sheep which was originally intended to become a non-union. Insufficient fixation stability indeed led to the development of a hypertrophic pseudarthrosis in some animals, but it was not reproducible in all. This conclusion could only be drawn by analyzing a longer term group with a healing time of six months. Therefore, it seems mandatory in establishing a hypertrophic pseudarthrosis to verify the cessation of the healing by inclusion of a longer term group. Despite the failure in mechanical induction of a reproducible non-union, the ovine model presented in this study offers the option for investigations of the patho-physiological healing processes occurring in fracture repair leading to delayed or even non-union. By mechanical induction of critical healing using an external fixation device, the healing cascade may be investigated without suffering from any biological intervention.