Introduction: Articular cartilage is a specialized connective tissue with limited capacity for self regeneration. The function of articular cartilage depends on the mechanical support of subchondral bone [1]. Critical osteochondral defects fail to heal spontaneously because of the imbalance of mechanical conditions at the base of the defect [2]. Therefore, restoration of the subchondral bone is believed to be important for bone and cartilage regeneration. Scaffolds offer an alternative to grafts in the treatment of osteochondral defects. This study investigates the influence of scaffolds stiffness on subchondral bone regeneration and the subsequent regeneration of cartilage. It was hypothesized that a stiff scaffold creates better conditions necessary for bone formation and cartilage regeneration than a more flexible one.

Materials and Methods: Critical osteochondral defects (7.3 mm in diameter) were created in the weight-bearing region of the left hind limb of 24 sheep. Defects were filled with either a commercial biodegradable polylactide-co-glycolide scaffold or a modified softer one (87% and 55% of the elastic modulus of ovine subchondral bone, respectively). Empty defects served as an untreated control. The mechanical properties of the regenerated tissue at the defect surface were determined with indentation testing using a high-precision material testing device mechanical at 3 and 6 months postoperatively (n=6). The morphology of tissue filling the defects were determined with histological and histomorphometrical techniques using Safranin O van Kossa, Masson Goldner trichrome and Safranin O light green staining and the HSI-based binarization mode taking into account the hue, saturation, and intensity.

Results: At 3 months, the elastic modulus of fibrocartilage in the stiff scaffold group (61% of healthy cartilage) tended to be higher than in the group treated with the softer scaffold (46%). The mechanical properties in both treated groups were similar at 6 months and not dissimilar to that of the tissue formed in the untreated specimens and well below that of healthy cartilage. No difference was determined at 6 months, but all were well below healthy cartilage. Untreated defects and defects treated with softer scaffolds showed less defect filling (91%, 93%) than those treated with stiff scaffolds (97%) at 3 months. At 6 months, defect filling was similar for all defects. Untreated defects were characterized by cystic formation at the base of the defect and sclerosis of subchondral bone (Fig.1a,b). Substantial degradation of the softer scaffold was observed with sclerotic bone surrounding the softer scaffold (Fig.1c,d). Degradation of the stiff scaffold was slower and with continuous osseous replacement (Fig.1e,f).

Discussion: To perform a rigorous evaluation of the scaffolds, a critical defect was created in a large animal model. The lack of spontaneous healing, characterized by cystic formation at the base of the untreated defect and the subchondral sclerosis confirmed that the defect size was indeed critical. The stiff scaffold was found to improve the regeneration of subchondral bone in comparison to untreated defects. Osteochondral defects treated with stiff scaffolds were characterized by trabecular bone formation with continuous osseous replacement of the scaffold. The softer scaffolds provided less support and as a consequence the surrounding subchondral bone became sclerotic. The differences seen in subchondral bone regeneration did not however, translate into differences in cartilage regeneration. The time-related changes during implant degradation may have affected cartilage regeneration. If degradation occurs too rapidly, as in the case of the softer scaffold, then the new formed bone near the joint surface looses its underlying support and may partially collapse into the defect. As a consequence, the loading of the overly-regenerating cartilage will be affected possibly leading to adverse conditions for regeneration. The results imply that subchondral defect filling in clinical settings advances bone regeneration and should have a stiffness which is similar to subchondral bone rather than being more flexible. However, there are some risks associated with the use of biodegradable implants [3] as the time-related changes in the implant stiffness in this study.

Acknowledgements: OsteoBiologics, San Antonio, TX, for supplying scaffolds. This study was supported by a grant of the German Research Foundation (DU 298/8-3).

Figure 1: osteochondral defect healing at 3 (left side) and 6 months (right side) with bone sclerosis around an untreated defect (a, b) and around defects treated with a softer scaffold (c, d), as where the stiff scaffolds showed continuous osseous replacement (e, f) (scale bar 2mm, Safranin-o von Kossa).