7 Summary

Influence of pluripotent mesenchymal stem cells on bone healing in a rodent atrophic nonunion model regarding the periosteal reconstruction.

Atrophic nonunions represent one of the most severe complications in fracture healing. The bone´s biological capability to heal is such reduced, that it necessarily needs any external support. Often the refreshment of the ends of fragments, switching osteosynthesis and transplantation of spongiosa is necessary. Besides high economic costs the patient suffers a considerable restriction of quality of life. Futhermore an increasing operation risk and donor-site morbidity may result from switching osteosynthesis and transplantation of spongiosa (Arrington et al., 1996). Therefore in this study was investigated, how far local injected autogenic mesenchymal stem cells impact the early healing of an osteotomy with reduced biological potential. Futhermore, findings about the so far unknown course of periosteal reconstruction during bone healing should be gained by analysing the role of the injected cells in periosteal reconstruction. Therefore 32 rats were randomised into two groups. After sampling of bone marrow and selection of the bone marrow´s mesenchymal stem cells took place, a standardised osteotomy of the femur´s midshaft, which was stabilised with an external fixator was performed. In order to produce the atrophic nonunion, the periosteum was cauterized circumferentially for a distance of 2 mm on each side of the osteotomy. In this area the bone marrow was removed. Two days after the osteotomy 16 animals got a percutaneous injection of 2 x 10^6 MSCs/100 µl cell-medium-suspension in the osteotomy gap (msc-group). The other 16 rats served as control group. These animals obtained the equivalent volume of the expansion medium without cells (medium-group). X-rays were taken directly after operation and in weekly intervals. Two weeks after osteotomy the femora was extracted for histological, immunhistological and histomorphometrical examination of the osteotomy area. In both groups the course of healing appeared delayed as well radiologically as histologically. The histological appearances were equal in both groups. The callus tissue in the cauterised area of the msc-group differentiated more often into cartilage tissue. The histomorphometrical ananlysis shows, that the bone area, the mineralised area, the connective tissue area, and the cartilage area of periosteal callus of the msc-group were significantly greater. Relating to the total callus area these differences balanced. Both groups were equal regarding all other analysed parameters. The injected stem cells neither contributed to bone healing nor did they influence periosteal reconstruction. In both groups the fibrous layer of

periosteum started to reestablish discreetly two weeks after osteotomy. The cambium layer of periosteum had not the ability to do so. Apparently the complete periosteal reconstruction is bound to the formation of an osseus callus.

Possibly the application of the cells at a later date (e. q. after establish of an atrophic nonunion) or the use of osteogen pre-differentiated cells would have lead to a more benefical course of healing.