Introduction: Many times, an osteoporotic fracture is the first event to consult a medical institution and induce the adequate medication to prevent further fractures. An osteoporotic fracture often leads to immobilization and a reduction of general condition with an increase of morbidity and mortality. Therapeutic treatments aim for faster mobilisation and reintegration of the patients in their everyday life. It is unknown if certain drugs may currently affect fracture repair in osteoporotic patients and may accelerate the rehabilitation.

Besides the well-known and mostly prescribed bisphosphonates there are several other drugs such as PTH 1-34 and strontium ranelate. Both are considered to be anabolic. Intermittent substitution of PTH 1-34 causes an increase in bone mineral density by an enhancement of osteoblast proliferation. Strontium ranelate does not only enhance the activity of osteoblasts by activating the calcium sensing receptor but also causes a downregulation of osteoclast activity.

In the past, animal models were used to simulate clinical situations and answer specific problems. In female Sprague-Dawley (SD) rats, it is known that ovariectomy leads to osteopenia. Early in the 1980’s, T. Einhorn introduced a model of a standardized, closed diaphyseal fracture in rats. In this study, we wanted to see if PTH 1-34 and strontium ranelate affect fracture healing when given the first time after an osteoporotic fracture and if they show any benefit in stability of the callus. We combined the model of the ovariectomized rat with a closed diaphyseal fracture.

Materials and Methods: 45 Sprague Dawley rats were ovariectomized at the age of 12 weeks. After 12 weeks, an osteopenia was diagnosed using Dual x-ray energy (DXA). Under systemic anesthesia a 0.8 mm Kirschner wire was introduced into the femoral canal through a medial parapatellar incision and arthroscopy of the knee joint. After closing the wound a mid-diaphyseal fracture was produced using a falling weight of 650 g over a three-point bending mechanism. The fracture was radiographically documented. Afterwards, the animals were randomly put into three groups. The first group was substituted with 0,9% NaCl s.c., the second received radiographically documented. Afterwards, the animals were randomly put into three groups. The first group was substituted with 0,9% NaCl s.c., the second received radiographically documented. Afterwards, the animals were randomly put into three groups. The first group was substituted with 0,9% NaCl s.c., the second received radiographically documented. Afterwards, the animals were randomly put into three groups. The first group was substituted with 0,9% NaCl s.c., the second received radiographically documented. Afterwards, the animals were randomly put into three groups. The first group was substituted with 0,9% NaCl s.c., the second received radiographically documented. Afterwards, the animals were randomly put into three groups. The first group was substituted with 0,9% NaCl s.c., the second received radiographically documented.

The samples were scanned using MicroCT 80 by Scanco Medical, Zuerich, Switzerland. The whole bone was scanned and afterwards 600 40 micron slices were placed through the former fracture area. The evaluation of the data focused on outer callus contour, cortical contour and the marrow contour as well as the cortical thickness and the polar moment of inertia.

After embedding the samples in Technovit (Heraeus Sulzer) torsion testing on outer callus contour, cortical contour and the marrow contour as well as the cortical thickness and the polar moment of inertia.

The samples were scanned using MicroCT 80 by Scanco Medical, Zuerich, Switzerland. The whole bone was scanned and afterwards 600 40 micron slices were placed through the former fracture area. The evaluation of the data focused on outer callus contour, cortical contour and the marrow contour as well as the cortical thickness and the polar moment of inertia.

Data was collected in Excel (Microsoft). All data were expressed as the mean ± standard deviation. For statistical analysis, we used the one way ANOVA, p<0,05 was considered as being significant compared to the control group. Sigma Stat was applied.

Results: PTH 1-34 and strontium ranelate both showed an significant increase in bone volume of the callus. (strontium ranelate +46,4%, p<0,05; PTH 1-34 +31,9%, p<0,05) though difference among them was not significant. This was also

expressed in callus tissue volume (strontium ranelate +32,4%, p<0,05, PTH 1-34 +6%, p<0,05) while the increase under substitution with strontium was significantly higher (+ 24,8%, p<0,05). Polar moment of inertia, being a parameter which predicts an object’s ability to resist torsion was only significant under substitution with Strontium (+35%, p<0,05).

Mechanical testings showed no significant differences when practicing torsion to the yield point. Torsion to bone fracture was significant higher under substitution with strontium ranelate while substitution with PTH 1-34 showed no difference.

Discussion: Osteoporotic fractures in formerly untreated patients do mostly lead to an increased morbidity and mortality with the risk of being bedridden and suffering from further fractures. Being the first signs of osteoporosis, an adequate and evidence-based medication for osteoporosis needs to be induced. It is unknown, if certain osteoporotic drugs impair fracture healing or even may support the healing with the result of earlier mobilisation of the patients. Besides the substitution with vitamin D and calcium, bisphosphonates, estrogen, raloxifene, strontium ranelate and 1-34 PTH are commonly used drugs. Healing in osteoporotic bones is considerably reduced due to worse mechanical properties as well as the reduced primarily stability of osteosynthesis. Animal experiments in rats have shown a limited early phase of fracture healing when compared to non-osteoporotic animals. PTH 1-34 increase bone mineral density both in animal experiments as well as in human therapy. In animal experiments a continuous infusion of PTH 1-34 has catabolic whereas the intermittent substitution has anabolic effects on bone formation. Furthermore, it was shown in non-osteoporotic rats that daily administration of PTH 1-34 enhances fracture healing. Strontium ranelate is an orally administered agent and has also shown an increase of bone mineral density and a reduction of the fracture rate. Until now, it is unknown if strontium ranelate affects fracture healing. To our knowledge, no animal experiments were done to evaluate its influence of fracture healing. Our results show clearly that there is no negative effect on fracture healing of both therapeutics compared to the control group and that they may be taken into consideration as therapeutic drugs after fracture. Furthermore support our results that both PTH 1-34 and strontium may enhance fracture healing with an increase in callus tissue and bone volume. Callus in strontium substituted animals seems to be more resistant to torsion in comparison to sham-treated animals or animals being treated with PTH 1-34. Strontium had significant better results in torsion testing to the fracture point. This may be an effect from a higher callus volume and callus bone volume / tissue volume.


Acknowledgements: The animal experiments were approved by the Regierungspraesidium Darmstadt, Germany (F-119/04). This study was supported by the Elisabeth Bonhoff Stiftung.