

# BONE CARRIERS WITH MESENCHYMAL STEM CELLS

## SUMMARY

This thesis deals with certain issues relating to bone regeneration. It is divided into experimental and clinical parts. In the experimental part, the number, viability, and proliferative ability of mesenchymal stem cells obtained from the bone marrow of proximal femur of 24 female patients with hip osteoarthritis, who had already undergone a total hip arthroplasty implantation, were determined. At the same time, the incidence of osteopenia / osteoporosis in coincidence with hip osteoarthritis and their influence on the properties of mesenchymal stem cells were ascertained. The final outcome is a significant prevalence of low bone density and its coincidence with hip osteoarthritis, and moreover, when identical viability of mesenchymal stem cells, in bones with lower density, there is a smaller number and reduced proliferative capacity of such cells. In the second phase, the activity of mesenchymal stem cells in selected carriers was monitored. These cells were found either in the aspirate of complete bone marrow or in monocyte concentrate. From the carriers we tested cancellous bone allograft, demineralized bone matrix, porous  $\beta$ -tricalcium phosphate, molded hydroxyapatite and calcium sulfate. We evaluated the formation of collagen fibers and the mineralized extracellular matrix. We used expansion medium and osteogenic differentiation medium. At the same time, we compared the activity of mesenchymal stem cells during complete bone marrow application and during monocyte concentrate application. The most significant production of collagen and extracellular mineralized matrix was in the expansion medium for allograft, and less in the demineralized bone matrix. When bone graft substitutes with mesenchymal stem cells were present in the expansion medium, such a formation was not evident, thus we had to use the osteogenic differentiation medium, with the best results noted when  $\beta$ -tricalcium phosphate had been used. Furthermore, better results were achieved when applying complete bone marrow, rather than monocyte concentrate.

In the clinical part, we evaluated the healing of 87 bone defects in tumor-like lesions and benign tumors with an average volume of 15 cm<sup>3</sup>. 28 defects were filled with autologous bone grafts, 44 porous  $\beta$ -tricalcium phosphate (Poresorb-TCP®) and 15 combinations of both materials in a 1:2 ratio in favor of  $\beta$ -tricalcium phosphate. During the course of postoperative control, using radiographs we evaluated the filling resorption and the defect trabeculation. Comparing all three fillings we recorded a faster resorption phase, respectively, trabeculation up to 12th month after the operation, followed by a slower phase. In autologous bone graft resorption was only slight and trabeculation exceeded 70% in the 1st year post-operatively. In addition, we noted minimal complications harvesting grafts from the iliac crest. Poresorb-TCP® was well tolerated without any undesirable reactions, also in case of leakage into the soft tissues was fully absorbed with no complications. However, filling resorption, and material trabeculation was relatively slow. Comparable results were seen even in combinations of both materials, with evidently faster resorption as well as trabeculation only during the first six months, compared to Poresorb itself. Bone graft substitutes are so far inferior to autologous bone. In establishing criteria for successful healing - 80% trabeculation of the defect during the 1st year after the operation has been calculated as the borderline defect volume of 4 cm<sup>3</sup>, up to which trabeculation of the defect was similar, either filled with autologous bone grafts, or Poresorb-TCP®. There was no statistically significant dependence of the defect healing with age, or the location of the defect in the bone, with a predominance of cancellous, cortical, or cortical-cancellous bone. However, in clinical monitoring healing of defects in the diaphysis lasted longer. It was found deceleration of the defect trabeculation in cases of a simultaneously performed osteosynthesis and acceleration when progressively weight-bearing the concerned extremities.

Standard for filling bone defects remain autologous bone grafts. Poresorb-TCP® however, is a reliable substitute of bone grafts applicable in both children and adults. It can be used alone or together with bone grafts. The best results were obtained when filling defects with volume up to 4cm<sup>3</sup>.