Abstract:
The treatment of osteochondral articular defects has been challenging physicians for many years. The better understanding of interactions of articular cartilage and subchondral bone in recent years led to increased attention to restoration of the entire osteochondral unit. In comparison to chondral lesions the regeneration of osteochondral defects is much more complex and a far greater surgical and therapeutic challenge. The damaged tissue does not only include the superficial cartilage layer but also the subchondral bone. For deep, osteochondral damage, as it occurs for example with osteochondrosis dissecans, the full thickness of the defect needs to be replaced to restore the joint surface (1). Eligible therapeutic procedures have to consider these two different tissues with their different intrinsic healing potential (2). In the last decades, several surgical treatment options have emerged and have already been clinically established (3-6). Autologous or allogeneic osteochondral transplants consist of articular cartilage and subchondral bone and allow the replacement of the entire osteochondral unit. The defects are filled with cylindrical osteochondral grafts that aim to provide a congruent hyaline cartilage covered surface (3,7,8). Disadvantages are the limited amount of available grafts, donor site morbidity (for autologous transplants)...
and the incongruence of the surface; thereby the application of this method is especially limited for large defects. New approaches in the field of tissue engineering opened up promising possibilities for regenerative osteochondral therapy. The implantation of autologous chondrocytes marked the first cell based biological approach for the treatment of full-thickness cartilage lesions and is now worldwide established with good clinical results even 10 to 20 years after implantation (9,10). However, to date, this technique is not suitable for the treatment of all types of lesions such as deep defects involving the subchondral bone (11). The sandwich-technique combines bone grafting with current approaches in Tissue Engineering (5,6). This combination seems to be able to overcome the limitations seen in osteochondral grafts alone. After autologous bone grafting to the subchondral defect area, a membrane seeded with autologous chondrocytes is sutured above and facilitates to match the topology of the graft with the injured site. Of course, the previous bone reconstruction needs additional surgical time and often even an additional surgery. Moreover, to date, long-term data is missing (12). Tissue Engineering without additional bone grafting aims to restore the complex structure and properties of native articular cartilage by chondrogenic and osteogenic potential of the transplanted cells. However, again, it is usually only the cartilage tissue that is more or less regenerated. Additional osteochondral damage needs a specific further treatment. In order to achieve a regeneration of the multilayered structure of osteochondral defects, three-dimensional tissue engineered products seeded with autologous/allogeneic cells might provide a good regeneration capacity (11). Beside autologous chondrocytes, mesenchymal stem cells (MSC) seem to be an attractive alternative for the development of a full-thickness cartilage tissue. In numerous preclinical in vitro and in vivo studies, mesenchymal stem cells have displayed excellent tissue regeneration potential (13,14). The important advantage of mesenchymal stem cells especially for the treatment of osteochondral defects is that they have the capacity to differentiate in osteocytes as well as chondrocytes. Therefore, they potentially allow a multilayered regeneration of the defect. In recent years, several scaffolds with osteochondral regenerative potential have therefore been developed and evaluated with promising preliminary results (1,15-18). Furthermore, fibrin glue as a cell carrier became one of the preferred techniques in experimental cartilage repair and has already successfully been used in several animal studies (19-21) and even first human trials (22). The following protocol will demonstrate an experimental technique for isolating mesenchymal stem cells from a rabbit's bone marrow, for subsequent proliferation in cell culture and for preparing a standardized in vitro-model for fibrin-cell-clots. Finally, a technique for the implantation of pre-established fibrin-cell-clots into artificial osteochondral defects of the rabbit's knee joint will be described.