**Abstract**

Critical size bone defects are defined as those being more than 1.5 times larger than the bone diameter and do not heal if left untreated. This constitutes a major challenge for trauma surgeons, and to date, the gold standard treatment resides in the gap filling with autologous bone graft. Because of the low amount available, and the need of a 2nd place of surgery associated with increased pain and risk of infections for the patient, alternative methods are under investigation since about 2 decades that involve structural scaffolds associated with biological active components (cells, growth factors). Presently, rigid fixations are widely used for the management of all kind of fractures. However, over the past few years, increasing amount of experimental and clinical evidences report that the fracture healing can be influenced by mechanical loading. Yet, most of the data available are concerning small fracture gaps (≤2mm), simple osteotomies or distraction osteogenesis cases. Thus very little is known about the effect of mechanical stimulation when applied to a critical size bone defect. Questions concerning the timing, the amount, and the length of stimulation are still open. In the present study we aim to investigate the effect of axial mechanical loading on the healing of a critical size bone defect in the rat femur. In order to establish a favorable stimulation protocol, we will first treat the large bone defect with autologous/syngeneic bone graft (gold standard, positive control) to which different loading protocols will be applied. Once the optimal stimulation conditions will be determined, we will then move to a more complex but also clinical relevant model in which the defect will be treated with tissue engineered constructs aiming to promote bone formation and implant's neo-vascularization in parallel.