Fracture healing: A harmony of optimal biology and optimal fixation?

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Despite the substantial advances made in the understanding of the molecular mechanisms governing the fracture healing response, bone growth remains one of the major challenges of regenerative medicine\textsuperscript{, 4,8,9,13}. Bone tissue has regenerative abilities that allow self repair of fractures without any form of scarring. Conversely, there are situations where the extent of bone loss is too large for complete regeneration to occur\textsuperscript{.15}. Treatment of critical size bone defects is a clinical problem often encountered in young patients following severe open limb injuries. If bone growth fails then a variable degree of morbidity may prevail with the end point being amputation of the limb. In addition the demographic challenges of an increasingly aging population dictate the need for innovative approaches to skeletal reconstruction to augment and repair skeletal tissue lost as a result of implant loosening, trauma, degeneration or in situations involving revision surgery requiring bone stock.

The increasing demand of bone tissue is supported by the fact that an excess of 500,000 bone grafting procedures take place annually in the United States and 2.2 million worldwide. In the United States, the estimated bone grafts and bone substitutes market totalled $543.1 million in revenues in 2001, whereas in Europe the allograft and synthetic bone graft substitutes market was estimated at $39.5 million in 2003\textsuperscript{.5}. The current need for bone tissue augmentation and regeneration therefore has necessitated the development of a new science termed ‘bone tissue engineering’.

In order to achieve bone regeneration, a variety of concepts has been proposed and currently being investigated by researchers in the different parts of the world. Growth factors, such as bone morphogenetic proteins, engineered adult stem cells combined with scaffolds can be implanted into target sites, with or without ex vivo culture period\textsuperscript{.1,2,3,6,7,10,12,14,16,17}. Gene therapy is also becoming an attractive new approach and an increasing amount of evidence indicates that gene transfer can aid the repair of bone, articular cartilage, menisci, intervertebral discs, ligaments and tendons\textsuperscript{.11}. It has been shown that several important factors influence the success of bone engineering.
approaches including choice of cell and scaffold, the vector used in order to deliver the osteogenic gene, and the osteogenic gene itself. Sophisticated imaging technologies, bioinformatics-based analysis of gene expression and exogenous regulation of transgene expression are among the tools that are being used to optimize and control bone formation in vivo. Implantation of anabolic agents has the capacity to regulate and enhance the biological potential of different elements of the musculoskeletal system allowing restoration of movement and function. 17

In addition to the biological processes, bone-healing is also known to be sensitive to the mechanical stability of fixation. The application of Wolff’s law to the clinical setting of fracture healing together with the interplay between parameters as implant rigidity, relative or absolute fracture stability, fracture gap size, and interfragmentary strain are all efforts to express and determine the complex phenomena of bone fracture repair.

The role of mechanical stability in the microenvironments implanted applying tissue engineering approaches is also essential and often overlooked. These properties vary greatly among the various biomaterials and depend on topography and porosity. It is of paramount importance to improve initially the mechanical properties of the available biomaterials and to guarantee the presence of a mechanically reliable construct throughout all the remodelling phase of fracture healing. 7

Mechanical stability therefore should be given equal significance to the biologic properties of the graft itself whether it is the gold standard of autograft or synthetic grafting material. In this issue of Injury, all of the above elements have been given equal significance. Tissue engineering approaches therefore should not based on the concept of a triangular shaped model (cells, growth factors, scaffolds) but rather on a ‘diamond shaped’ concept of interaction (cells, scaffolds, growth factors and mechanical stability).

For this reason the 4th European Clinical Symposium on Tissue Engineering and Bone Regeneration is focused this year on the principles of optimal fixation and optimal biology. Our commitment to education and dissemination of knowledge is ongoing.

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Conflict of interest

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References