Role of the Subchondral Bone in Articular Cartilage Degeneration and Repair

The subchondral bone has long been recognized as playing an important role in articular cartilage repair. From an anatomic standpoint, the subchondral bone is the bony lamella that lies below the calcified zone of the articular cartilage, separated by the cement line. Trabeculae arising from the subchondral bone plate form a spongious network, the subarticular spongiosa. The term osteochondral unit reflects the close interaction between these two tissues of dissimilar intrinsic repair capacities. Here, we focus on novel translational data on the role of the subchondral bone in the development of osteoarthritis (OA) and in the field of reconstructive therapies for focal articular cartilage defects.

Role of Subchondral Bone in Early Osteoarthritis

OA is considered a disease of the entire joint, with biochemical and molecular crosstalk and signaling pathways between all affected tissues (ie, cartilage, bone, synovium, meniscus, capsule, ligaments, muscles), leading to abnormal joint remodeling by failure of the natural repair processes. Subchondral bone plays an important role early in the development of OA. In early OA, thickness of both the subchondral bone plate and subarticular spongiosa is increased, mineral content is reduced, and trabecular integrity is altered. Intriguingly, such a pattern co-localizes with regions of articular cartilage damage. Although the final primacy of these alterations remains to be determined, recent data show that when defined subchondral bone changes are established, articular cartilage damage may be induced. Systemic administration of PTH 1-34, the 1-34 amino acid segment of parathyroid hormone, induced an enhanced volume, mineral density, and microarchitecture of the subarticular spongiosa, together with a broadened calcified cartilage layer, in a previously normal osteochondral unit in vivo. Such alterations of calcified tissues may therefore lead to an instigation of early degeneration of the hyaline cartilage. These findings support the paradigm of a close crosstalk within the osteochondral unit under physiologic and pathologic conditions.

Relevance of Subchondral Bone for Reconstructive Cartilage Repair

Several pathologic features of subchondral bone emerge in a temporally precise fashion during spontaneous and therapeutic repair of chondral and osteochondral defects. These features include structural alterations of the subchondral bone microstructure, the advancement of the subchondral bone plate toward the joint line, the formation of intralesional osteophytes, and the appearance of subchondral bone cysts. Possible causes include, but may not be limited to, impaired osteochondral crosstalk and regeneration, pathologic consequences of altered biomechanical loading, and pathologic vascularization or angiogenesis. Many translational studies showed a lack of correlation between cartilage and subchondral bone repair, suggesting that independent repair pathways take place within these tissues. In
animal models, the subchondral bone plate advancement arises earlier in small animals but is more pronounced in the long term in large animal models. Clinical investigations have also demonstrated subchondral bone changes after cartilage repair. Although initially ascribed to marrow-stimulation techniques, such changes were also observed in the context of autologous chondrocyte implantation. These observations suggest that none of these different approaches for cartilage repair is superior with regard to subchondral bone pathologies.\textsuperscript{11}

Recently, strategies to diminish subchondral bone alterations were developed. Marrow stimulation is still the most commonly used cartilage repair procedure, but there is little consensus on basic technical parameters. Mechanistically, the procedure induces multiple standardized small bone injuries in the subchondral bone plate. Current data from translational models of marrow stimulation support the value of small-diameter instruments, in contrast to instruments with larger diameters.\textsuperscript{12} For example, small subchondral drill holes that reflect the physiologic subchondral trabecular distance improve osteochondral repair more effectively than do larger drill holes.\textsuperscript{13} Likewise, small-diameter microfracture awls improved articular cartilage repair in a translational sheep model more effectively than did larger awls.\textsuperscript{14} These data suggest that smaller subchondral bone perforations allow for a better reconstitution of the microarchitecture of the subchondral bone plate and subarticular spongiosa, although the dimension of the opening of the subchondral bone plate also proportionally affects the number of possible recruited mesenchymal stem cells (which, in theory, may accelerate cartilage repair). Altogether, these data support the use of small instruments for the surgical treatment of cartilage defects and have important clinical implications in the execution of marrow stimulation.

**Summary**

In light of recent studies, subchondral bone continues to provide important information about the development of OA. Results from several translational models demonstrate the critical importance of the structural integrity of subchondral bone because its protection improves reconstructive therapies for focal cartilage defects. Given the still incomplete understanding about the mechanisms of OA and cartilage repair, enhanced knowledge of the basic science and clinical events in this frontier region will likely translate into improved therapeutic strategies for osteochondral regeneration.

**References**

References printed in **bold type** are those published within the past 5 years.