Subchondral Bone: Healthy Soil for the Healthy Cartilage

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38.1 Introduction

It has been a classical teaching that cartilage is a load-bearing structure of the joint that doesn't have a nerve, blood, and lymph supply. In addition, the cartilage gets its nutrition only through osmotic diffusion from the synovial joint and hence has a limited opportunity of natural healing. The role of subchondral (SC) bone as a load-sharing structure and as a nutritional support has been heavily ignored in the medical literature.

The subchondral (SC) bone is an important structure present underneath the cartilage and comprises of two major parts: the subchondral bone plate and the subchondral spongiosa [1]. The SC bone plays an important role in natural healing of the cartilage through its various properties like nutritional properties, load-bearing properties and as a warehouse of cartilage cells and growth factors. While it is easy to understand the role of nutrition and the role of constant supply of cells and growth factors in the natural healing of cartilage, it is little tricky to understand the role of load bearing for the same. Ever since the interest in cartilage repair got renewed about two decades ago, the surgeons and the scientists continued to take care of the SC bone. However, most of this subchondral bone-specific attention was unintended attention.

Marrow stimulation techniques like microfracture (MF) relied on the SC bone for recruitment of the autologous stem cells and formation of a super clot. However, scientists ignored the

A. Gobbi et al. (eds.), *Bio-orthopaedics*, DOI 10.1007/978-3-662-54181-4_38

implications of MF holes on the SC bone that lead to thickened SC bone, SC cysts, and internal osteophyte post-MF. Similarly for the osteochondral cylinder transfer techniques; though the cylinderical osteochondral unit was transferred, the bone was merely used as a carrier and to provide a press-fit fixation. The technique stressed on the importance of articular congruency but never stressed the importance of the SC bone congruency. Autologous chondrocyte implantation technique continued to evolve in different generations but with a very little attention being paid to the subchondral bone reconstruction until recently [2].

Now as the attention is being paid to treat cartilage lesions as one osteochondral unit rather than treating the cartilage only [3], it is timely to establish the role of SC bone in the natural healing of the cartilage. It is important to understand that the articular cartilage and the SC bone are one functional unit and are interdependent [4].

38.2 Role of Subchondral Bone in Natural Healing and Natural Protection

38.2.1 Nutritional Support

Traditionally, it is believed that cartilage gets its nutrition through diffusion from the synovial fluid. However, there is a substantial evidence to support the presence of a vascular supply from SC bone to the cartilage that plays a role in the natural cartilage healing. Way back in 1929, Fisher [5] demonstrated the presence of porosity in the SC bone plate. Since then, there have been quite a few studies trying to prove the presence of vascularity beyond the SC bone into the cartilage. Berry's [6] study showed the presence of deficiencies in the SC bone plate extending into the basal cartilage. Imhof et al. [4] showed the presence of canals penetrating the SC bone plate and reaching into the calcified cartilage layer up to the tidemark. These canals contained the arteriovenous complexes as well as the nerves. The arterial branches are probably end-arteries that end in sinusoids, and the sinusoids terminate in the venules. This study proved that the basal layer (calcified) of the cartilage has got a normal blood supply that can play an important role in the natural healing. The distribution of channels in the SC bone plate that extend into the calcified cartilage actually depends on the compressive forces that act on the cartilage and SC bone. Irrespective of age, more vessels are present in the load-bearing areas of the articular cartilage than in the other areas [4]. The blood flow rate in the SC plate has been shown to be 3–10 times higher than in the cancellous bone [7].

While there is a substantial evidence from the above studies that there is presence of arteriovenous complexes in the calcified cartilage, further studies are required to prove that the uncalcified cartilage also gets nutrients form the SC bone. Lyons et al. [8] showed that diffusion of nutrients does take place from the SC bone to the uncalcified cartilage. Various villous like projections were identified penetrating the calcified cartilage towards uncalcified cartilage from the SC bone and vice versa. Pan et al. [9] demonstrated presence of zones that allowed sodium fluorescence getting permeated into the uncalcified cartilage using the FLIP technique.

This specific SC bony micro-architecture thus proves that an absolute barrier to diffusion of nutrients between articular cartilage and SC bone doesn't exist [4]. The SC bone actually allows a direct supply of nutrition to the calcified cartilage through small vascular channels while it also allows indirect supply of nutrition to the uncalcified cartilage by permeable diffusion. It is obvious that this nutritional supply plays an active role in the natural healing that is required after day-to-day wear and tear.

The study by Lane et al. [10] further supports this theory. They demonstrated higher vascular perforations at the areas of higher stress, indicating that the SC bone responds to non-physiological loads by increasing the blood supply and thereby helping in the healing process. The increased loads lead to an increase in the nutrient supply, thereby helping in sustaining the loads and natural healing. However, abnormally high loads or overloading on the degenerated joint will impede the flow of nutrients from the SC bone to the cartilage and thus won't help in natural healing.

38.2.2 Load Bearing

Cartilage is considered as a load-bearing structure of the joint. However, with its limited regenerating capacity, cartilage cannot survive long if it had been the principle load-bearing structure. The presence of extensive bone marrow edema and architectural breaks in the SC bone on MRI in post-trauma cases is enough evidence to prove that SC bone is an equal load-bearing structure. The osteochondral unit should work as a single unit to bear the daily physiological loads and should also allow a physiological and a structural equilibrium to heal. The SC bone should act as a dynamic component of the OC unit that transmits forces through the joint and adapts to its mechanical needs [11].

The joints in the lower limb bear more loads as compared to the joints in the upper limb. Even two different joints in the lower limb will bear different loads due to their size and proximity to the ground. Also, different areas of a joint bear different loads due to the angular forces acting on them. The cartilage has a poor regenerating capacity while the SC bone has a good regenerating capacity; however, both can only heal when the forces acting on them are minimized and are within the physiological limits. The unique structure of the OC unit has different properties in different layers that helps to minimize and redistribute the angular, shear, and vertical forces. Each microscopic structure of the SC bone–cartilage complex thus plays a vital role in the natural healing. Each of the microscopic structures with its unique properties is discussed here.

38.2.2.1 SC Bone Spongiosa

The bony trabeculae present in the SC spongiosa are architectured to bear the compressive forces and the tensile forces in the form of compression and traction trabeculae, respectively. Both the trabeculae play an important role in bearing the angular loads acting on the joint. A physiological load put on the joint is absorbed by these trabeculae while any abnormal load can lead to an injury to these trabeculae. Microfractured trabeculae remodel fast to provide healing to the stressed OC unit, while also prepare itself for further stresses.

38.2.2.2 SC Bone Plate

The most concave part of the joint bears the maximum load as different forces get concentrated at this point. To withstand higher forces, the bone plate at this point should be strong as well as dense. The strength and density can be measured in terms of the bone thickness and the bone mineralization, respectively. Milz and Putz [12] measured the thickness of the proximal tibial articular bone plate and found that it is thickest in the most concave parts of the medial and the lateral tibial plateau. The thickness at the periphery of the plateau was measured as 100 μm while at the most concave portion was around 900 μm. Hoechel et al. [11] demonstrated that computed tomography osteoabsorptiometry (CT-OAM) is a good method to determine mineralization of the bone; thereby reflecting the density of the bone. Hoechel et al. [11] mapped the strength distribution of human patella and correlated it to the SC bone plate density using CT-OAM. The 20 human patellas that were studied showed a non-homogenous distribution of the bone density and the mechanical strength. However, both the density and the mechanical strength had a regular reproducible picture which mirrored a long-term stress distribution pattern on the articular surfaces. It is a known fact that the lateral patellar surface has a greater contact area than the medial patellar surface during knee flexion, suggesting a higher load being put on the lateral patellar surface [13]. Hoechel et al. [11] results revealed that 19/20 patella had maximum bone density values at the lateral patellar facet that fall off towards the periphery. The mechanical strength distribution tested by the indentation technique revealed a similar distribution pattern as CT-OAM did for density. The minimum force needed to penetrate the SC bone plate was shown to be below 30 N in the periphery reaching 1034 N in the areas with the highest density. A direct correlation between the determined density values and the penetration force values of all the measuring points was found for every sample. A similar correlation has also been found in the glenoid cavity SC bone plate by Kraljević et al. [14].

Muller-Gerbl et al. [15] compared the thickness of the bone with the density of the bone thereby comparing the strength of the bone with the mineralization of the bone. The areas of the proximal tibial plateau that were dense were also more thick. These studies conclude that the SC bone plate responds to stresses by increasing its thickness and density. Muller-Gerbl study also showed that in the presence of genu vara, the SC bone plate thickness changes from more thick in the center of the medial plateau to more thick at the medial part of the medial plateau [1]. However, the bone thickness gradually reverts back to normal post-alignment surgery. Using CT-OAM, Egloff et al. [16] also demonstrated more dense SC plate in the posterolateral part of the talar body in the patients of valgus ankle osteoarthritis that decreased to normal after a re-alignment (supramalleolar osteotomy) surgery.

The density distribution of the SC bone plate not only gives information about higher mineralization but also about high osteoblastic activity, which is a reflection of its attempt to adapt to higher forces and heal naturally. This "extrinsic repair mechanism" depends on the response of loading by the SC bone plate, the spongiosa, and the calcified cartilage [4].

38.2.2.3 Calcified and Uncalcified Cartilage

There is a constant remodeling process going on at the calcified cartilage. The vessels invading the calcified cartilage from the SC bone brings osteoblasts, which synthesize bony tissue at its base. On the other side, the calcified cartilage advances into the uncalcified cartilage, while maintaining its own thickness. This constant remodeling is triggered by loading and unloading of the joint, and thus simultaneously helps in natural healing at the base of the cartilage from injuries occurring within the physiological limits.

The general orientation of the collagen fibrils in different layers occurs in response to the pressure, the traction, and the shear forces [4]. The orientation of the fibers is supported by the water and the proteoglycan content, which also support against the various forces. Proteoglycans present in the cartilage also exert an osmotic pressure to draw water into the cartilage, which counteracts the mechanical pressure put on it [4]. Apart from the osmotic diffusion from the joint fluid, the uncalcified cartilage also gets a permeable diffusion from the SC bone through villous-like formations [8, 9]. Moreover, loading encourages an increased synthesis of the proteoglycans and the fibrils by the chondrocytes. This "intrinsic repair" mechanism not only helps in the natural healing, but also counteracts the destructive loading process. As long as the loads are not beyond the critical capacity, the hydrophilic proteoglycans can withstand the loads and maintain the equilibrium necessary for a natural healing. Beyond a critical point, proteoglycans' breaks leading to changes in its' structures and other proteins.

The cartilage thickness varies from joint to joint and in different regions of the same joint. Smaller joints like ankle and subtalar joints have much thinner cartilage than the larger joints like the knee. A congruent joint requires a less thick cartilage even though it is small in size as compared to an incongruent joint. Osseous congruency is also different from the chondral congruency as evident from the study by Milz et al. [17]. The differences in the chondral congruency is to compensate the osseous congruency. This adjustment between the chondral and the osseous congruency is basically needed for an equal distribution of forces across the joints. During physiological loading and unloading, all the units of the OC unit deform with the most deformation taking place in the region of uncalcified cartilage [4]. Adjustments in the chondral and the osseous congruency, thus helps the uncalcified cartilage to deform more, threby increasingthe contact area of the osseous congruent area [4]. As long as the loads are distributed properly within the physiological limits, the cartilage can manage its equilibrium and heal within the physiological limits. Cartilage will not heal if the loads are beyond the physiological limits and then will start disintegrating.

38.2.2.4 Tidemark

The tidemark is the transition zone between the calcified cartilage and the uncalcified cartilage. Tidemark is not a linear structure but a micro-trilaminated structure, very much similar to the egg basket. This structural uniqueness helps in reducing the shear forces remarkably, that act on the osteochondral unit. In addition, type II collagen fibrils cross the tidemark. This uniqueness in the structure of the tidemark and the collagen fibrils provides a gradual transition between two dissimilar types of the cartilage (mainly calcified and the uncalcified cartilage). Again, the shear forces within the physiological limits will be very well countered by the tidemark, and hence it will allow the cartilage to maintain its physiological equilibrium of healing.

38.2.2.5 Cementing Line

No collagen fibrils cross the cementing line and thus the junction between SC bone and the cartilage is the weakest point in the OC unit.

38.2.3 Warehouse of GF and Cells

Chondrocytes are the main elements of cartilage; however, they originate from the undifferentiated mesenchymal marrow stem cells. These cells convert into chondroblasts while passing through the calcified cartilage, and then further convert into chondrocytes in the uncalcified layer and get isolated in the lacunae. Chondrocytes in the lacunae are, in fact, prisoners in their own home. They can divide but cannot proliferate. Hence the bone marrow stem cells continue to be the only source of fresh chondrocytes. Without the ability of the SC bone to provide the undifferentiated stem cells, and their further ability to differentiate into the chondroblasts, the natural healing of a day-to-day wear cannot take place.

Apart from being a warehouse of stem cells, SC bone also has a unique ability to provide endless supply of the growth factors. The various growth factors like IGFs, BMPs, FGFs, and TGF-B are in abundance and play a continuous role in the remodeling process and in the cartilage healing.

38.3 Discussion

The subchondral bone has an important and definitive role to play in the natural cartilage repair. Relationship between the cartilage and the subchondral bone is very much similar to the relationship between a plant and the soil underneath. We continue to learn from nature and use the knowledge in applied sciences. A healthy plant cannot be imagined without the healthy soil. The soil provides the base for the plant, a scaffold for its roots, supplies nutrition to it, and also gives it an ability to withstand the strong winds (shear forces) to avoid being uprooted. On the other side, the palnt provides the necessary coverage to the soil, so that the soil erosion is prevented from the direct stresses of harsh weather, and keeps the soil bound together with its roots. In a similar fashion, SC bone provides a strong base for the overlying cartilage, provides scaffold to the collagen fibers, supplies necessary nutrition, and provides the ability to withstand the shear and the compressive forces acting on the cartilage. The cartilage, in turn, provides the necessary covering to the articular bone, acts as a shock absorber, and plays a vital role in maintaining the biomechanical and the physical equilibrium. Figure 38.1 is a very good example to understand the soil–plant relationship vis-à-vis SC bone-cartilage relationship. As there is natural erosion of different layers of soil, the plant above is getting uprooted and destroyed. Soil is actually made up of four layers: topsoil, subsoil, regolith, and the rock bed. On top of these four layers, there is the covering by an organic layer and by plantations. An osteochondral unit also consists of calcified cartilage, cement line, subchondral bone plate, and the subarticular spongiosa; all the four layers having a superficial covering of articular cartilage.

Certain diseases of the cartilage are actually the diseases of the subchondral bone rather than the disease of the cartilage per se. It is akin to a bad soil causing loss of healthy plantation on it. Osteochondritis dissecans (OCD) is one such disease where the pathological process starts in the SC bone, gradually causing the separation of the affected bone from the surrounding healthy SC bone. An unstable and probably unviable SC bone causes the overlying cartilage to stop functioning in its normal capacity. Gradually, the whole OC unit separates with the overlying cartilage. A similar disease process occurs with osteonecrosis. Compare it with a condition in the backyard garden, where a disease affects the soil first. For example, an area of soil gets desiccated (state of extreme dryness due to lack of water)

Fig. 38.1 The soil-plant relationship vis-à-vis the subchondral bone-cartilage relationship. As the different layers of the soil are being eroded, the plantation above is getting uprooted. Similarly, an unhealthy subchondral bone can cause damage to the overlying cartilage. Also look at the more compact and closely woven layers of the soil near plantation; a similar relation exists between subchondral bone plate and the calcified cartilage. (Photo courtsey: Dr Deepak Goyal; on the banks of river Brahamputra, Assam, India.)

leading to loss of the entire healthy plantation on it. Any attempt to salvage the dying plant is useless unless a proper treatment for the ailing soil is done. If the desiccation process continues, the desiccated soil gradually separates from the surrounding soil. A dried up piece of soil that was devoid of water actually becomes useless and need to be replaced by the fresh soil. This is simply because of the reason that a soil deprived of water has also lost many nutrients and thus has also lost its regenerating capacity. OCD is a similar condition where the OC piece becomes sclerotic and fragmented. Any surgical attempt that can restore the vitality of the SC bone, before the desiccating fragment gets separated can actually provide a chance of regeneration. However, any attempt to fix the desiccated fragment usually doesn't restore the vitality of the OC unit since there is no attempt to heal by the SC bone.

Cartilage plays a protective role for the underlying bone from the stresses put on the joint. Similarly, the SC bone has a supportive role to play for the cartilage. This is a synergistic role where both work in a perfect homeostatic balance and neutralize the abnormal stresses acting on each other. Any isolated chondral injury or an isolated SC bone injury can alter the homeostatic balance of the joint, leading to the progression of the damage to the SC bone or the cartilage, respectively. An isolated chondral injury can make the osteochondral unit more vulnerable to the shear forces; which can gradually lead to increase in the size of the chondral defect and changes in the otherwise normal underlying SC bone plate in form of either overgrowth or bone loss [3]. Here, the protective role of the cartilage is lost that leads to the damage to the underlying bone. On the other hand, a subchondral bone fracture also leads to changes in homeostatic balance of the joint. Here, a supportive role of the SC bone is lost leading to a damage to the overlying cartilage. There are similar incidences where the soil is normal but there is loss of overlying plantation, thus exposing the soil to the harsh weather conditions. An exposed superficial area of land gradually gets eroded due to the shear forces of the strong winds. Gradually, the roots of the dead plants fail to keep the soil intact and cause loss of the soil crust. On the other side, a healthy and integrated soil is a must for a healthy plant. It provides a structured support for plant to grow. Any break in the soil crust can result in the loss of support of the overlying plant.

Qiu et al. [18] observed in their animal study that the SC bone started to advance towards the articular surface after lesion preparation and drilling of the cartilage defect. However, they noted that at 32 weeks, the regeneration of the bone continued to advance beyond the limits of the surrounding SC bone thereby leading to a thinning of the overlying well-grown cartilage. Perhaps, a proper check for the growth of advancing SC bone was not achieved. The authors hypothesized that a properly reconstructed SC bone can act as an efficient check for the further advancement of the regenerating bone. In another study by Orth et al. [19], SC drilling deteriorated the micro-architecture of both the SC bone plate and the spongiosa in the form of SC bone cysts, intra-lesional osteophytes, decreased bone volume, and bone mineral density.

Goyal et al. [20] in their meta-analysis concluded that MF gives good result for up to 5 years with patients having small lesions and low post-operative demands. Beyond 5 years, a treatment failure should be expected regardless of the lesion size. Study of Qiu et al. and Goyal et al. reveals a contrasting fact; access to the bone marrow through the SC bone is important to have undifferentiated stem cells, but same step is responsible for the failure of the repaired cartilage. Somewhere the SC bone and the bone marrow has a stimulating role for the cartilage repair but we still need to learn to check the same regenerating process once enough cartilage is regenerated.

Conclusion

The subchondral bone and the overlying cartilage work as one integral unit and help each other in maintaining the biomechanical equilibrium. The SC bone plays a vital role in supplying nutrition to the cartilage, in load bearing the stresses that occurs on the cartilage, and in providing a constant supply of pluripotent stem cells and the growth factors to the cartilage. All these functions of the SC bone help the cartilage in natural healing when demands are within the physiological limits. There is always an attempt by the SC bone to heal the damaged cartilage if it gets damaged by the forces beyond the physiological limits; however, it may not always succeed. A proper attention to the subchondral bone is thus important to maintain a healthy cartilaginous tissue under the physiological stresses and to regenerate a healthy cartilage in case of cartilage damage.

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