

The pathology and science of articular cartilage repair

Anjali Goyal^{1*}

¹Professor, Smt. N.H.L. Municipal Medical College, India

*Author for correspondence:
Email: anjali@knee.in

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Editorial

The adult articular cartilage is a specialized connective tissue, devoid of blood vessels, lymphatics, and nerves, hence has a limited capacity for intrinsic healing and repair. The cartilage around the knee joint has the following forms of cartilage- hyaline/articular, fibroelastic cartilage around the meniscus and fibrocartilage at the tendon and ligament insertion into the bone.

The science and dynamics of the articular cartilage around the knee joint is particularly important because of the increasing incidence of cartilage damage at an early age following lifestyle changes, overuse, injury, and accidents; subsequently leading to an early onset osteoarthritis.

The articular cartilage of the knee joint is a specialized form of hyaline cartilage which forms a smooth, white tissue covering the ends of the bones near the joint surfaces, transforming the articulating ends of the bone into lubricated, waterproof, and slightly compressible surfaces exhibiting very little friction. The only source of nutrition to the articular cartilage occurs by diffusion from the synovial fluid which fills the joint cavity, along with the small amounts of nutrients derived from blood vessels which course through the calcified cartilage close to the subchondral bone [1].

In addition to providing a smooth, lubricated surface for articulation, the articular cartilage around the knee joint helps in transmission of load with a low frictional coefficient. The stress shielding of the solid matrix components is due to a high-water content, incompressibility of water, and the structural organization of the proteoglycan and collagen molecules.

The articular cartilage chiefly comprises of (>95%) extracellular matrix (ECM) water, collagen, proteoglycans, and non-collagenous proteins with only a small percentage of chondrocytes (<5%). Whereas collagen (mainly Type II) and GAG (Glycosaminoglycans) mainly help in chondrocyte nutrition, the proteoglycan aggregates help in weight bearing.

The main component of the ECM is water (65-80%), with a higher proportion at the surface than at the deeper zones. The flow of water across the articular surface helps to transport and distribute nutrients to chondrocytes, in addition to providing lubrication.

The water content decreases with normal aging and increases in osteoarthritis, leading to an increased permeability, decreased strength, and reduced elasticity.

The two major load-bearing macromolecules: collagens (chiefly type II) and proteoglycans (notably, aggrecan), which form large aggregates with hyaluronan to hold water. The collagen molecules (chiefly type II), act to constrain the proteoglycans and help to hold their structure. This helps the cartilage to respond to the tensile, shear and compressive forces experienced by the cartilage during mechanical stress as in normal gait or weight bearing movements. Glycoprotein lubricin present in the superficial

layer of cartilage plays a role in bio-lubrication and wear protection of the cartilage.

The articular cartilage at the knee joint is divided into layers—graded according to their anatomy and function, from the deep layer adjacent to the subchondral bone to the superficial layer at the synovial surface. The tidemark separates the layer of calcified cartilage adjacent to the subchondral bone from the basal layer of cartilage.

Functionally, the superficial zone provides protection to the deeper layers and is responsible for the tensile properties of the cartilage, enabling to resist the shear and compressive forces. The middle and deep zone provides a resistance to the compressive forces and transmits the forces to the underlying subchondral bone owing to the perpendicular arrangement of the collagen fibers traversing the tidemark. The underlying zone of calcified cartilage defined by the tidemark helps in securing the cartilage to the underlying subchondral bone [1].

Chondrocytes make up only <5% of the total volume of the articular cartilage and originate from mesenchymal stem cells. They produce collagen, proteoglycans, and enzymes.

They respond to both mechanical (mechanical load, hydrostatic pressure change) and other stimuli like growth factors and cytokines.

The chondrocytes establish a specialized microenvironment and is responsible for producing collagenous extracellular matrix rich in Proteoglycans in its immediate vicinity, which traps the chondrocyte within its own matrix and so prevents any migration to adjacent areas of cartilage thus resulting in a limited intrinsic healing of the cartilage in response to injury.

Dynamics – Articular Cartilage

The chondrocytes are protected from the potentially damaging biomechanical forces by the surrounding ECM. Joint motion and load are important to maintain normal articular cartilage structure and function, hence an inactivity of the joint has been shown to lead to the degradation of cartilage.

The development of diseases such as osteoarthritis is associated with dramatic changes in cartilage metabolism resulting from a physiological imbalance of degradation and synthesis by chondrocytes [2].

Effect of loading- Repetitive loading like moderate running increases cartilage thickness and proteoglycan content. Extremes of use, ranging from strenuous loading or immobilization leads to cartilage thinning and proteoglycan loss.

Advanced glycosylation end-products (AGE) are formed due to a spontaneous nonenzymatic glycation of proteins and accumulate in the cartilage because of the low turnover of the articular cartilage. This is thought to play a role in the development of age-related osteoarthritis, by causing a modification of the collagen molecules and increasing the stiffness and brittleness resulting in an increased susceptibility to fatigue failure [3].

In addition to this, the other age-related changes include an increase in the chondrocytes size, protein content causing an increase in the forces transmitted to the subchondral bone seen as a subchondral sclerosis on MRI, along with a decrease in the absolute number of cells, water content, and the cartilage elasticity is seen [4].

The articular cartilage is frequently injured and has a limited capacity for repair attributable to avascularity of cartilage, immobility of the chondrocytes, and limited ability of mature chondrocytes to proliferate [5].

Superficial lacerations do not show healing due to the avascularity of the cartilage. The deep lacerations extending through the tidemark (separating the calcified from the non-calcified basal layer of the articular cartilage) hence have a fibrocartilaginous healing (rather than the hyaline cartilage), produced from the undifferentiated mesenchymal stem cells in the marrow. The response is initiated with a hematoma formation with a stem cell migration and vascular ingrowth. The resulting fibrocartilage (having type I collagen) has a reduced resiliency and stiffness causing a predilection for the development of arthritis. Hence, focal articular cartilage defects are progressive leading to deterioration, and an early diagnosis and treatment recommended prior to the development of more advanced osteoarthritis.

The extent of collagen type II in cartilage is considered a marker of the degree of differentiation toward hyaline cartilage and thus could represent a measure of good cartilage repair.

Therefore, focal damage to the articular cartilage at an early age needs to be treated to prevent the development of arthritis. The various techniques used include the marrow stimulation techniques like microfracture (resulting in a predominantly fibrocartilaginous healing), The osteochondral cylinder transfer techniques, and autologous chondrocyte implantation (ACI) techniques are the evolving techniques which require an expert set up in addition to being expensive).

The ACI, which deals with the implantation of autologous chondrocytes helps in the regeneration of hyaline like repair cartilage. However, it is associated with a two-stage procedure (chondrocyte harvesting and culture followed by chondrocyte implantation) and requires an ethical approval [6].

The latest development in the field is the use of chondroprogenitors and allogenic stem cells transplantation which can be injected into the damaged joint and are directed to help in the formation of hyaline repair cartilage. This would help in revolutionizing the field of cartilage repair.

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