Articular cartilage

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Abstract

Cartilage is a resilient structure that is both strong and flexible, and is found in many parts of the body. The type of collagen present in the structure determines the type and properties of the cartilage. The structure of articular cartilage is important for loading responses and lubrication, and a typical curve can be demonstrated for both stress-strain and creep-time properties. Osteoarthritis is a common post-traumatic consequence of articular cartilage injury as well as a well-known consequence of the ageing process. Different approaches to managing cartilage loss or injury have been explored and include steroid and hyaluronic injections, chondroplasty and chondrocyte transfer, with varying success.

Keywords articular; cartilage; chondrocyte; collagen

Introduction

Cartilage is found in many structures throughout the body and negotiates the balance between the need for structural support and flexibility in a unique fashion. It takes on different forms depending on the particular demand of the structure, and whilst the basic components of extracellular matrix and cells remain consistent, the proportions of these components vary within the cartilage subtypes.

Cartilage is formed by chondroblasts, which are mesenchymal in origin and which later mature into chondrocytes. Chondroblasts are thus typically found under the perichondrium along the border of the cartilage plates where new appositional growth occurs, although cartilage can also expand *via* interstitial growth. In epiphyseal plates, chondrocytes enlarge and divide during maturation to form single or multicellular lacunae arranged in linear stacks.

There are five recognized types of cartilage (with typical locations in brackets): hyaline (articular), fibroelastic (meniscus), fibrocartilage (bony insertion of tendon/ligament), elastic (trachea) and physeal cartilage (physis).

Healthy hyaline cartilage has a smooth, uniform, glassy appearance and is bluish-white in colour, but may loose some of these characteristics with age. The optical density of the collagen fibres approximates that of the extracellular matrix and they are therefore difficult to differentiate under light microscopy as structures separate from the matrix. Perichondrium covers hyaline cartilage and the chondrocytes are evenly distributed in lacunae. Hyaline cartilage provides the surface coverage of articular surfaces and is also found in the tip of the nose.

Elastic cartilage is more opaque and has a yellowish appearance. It is identified microscopically by clearly visible dark-staining elastic fibres embedded in ground substance and it is the presence of these fibres that is the most reliable means for differentiating elastic from hyaline cartilage. Perichondrium is also typically found around elastic cartilage. It is more elastic than other cartilage types and can be found in the epiglottis and external ear, where elasticity of tissues is essential.

Fibrocartilage contains fine collagen fibres arranged in layered arrays. Compared to the regimented appearance of hyaline cartilage, fibrocartilage appears more disorganized, with gaps between the lacunae and collagen fibre bundles. It is this open, more flexible structure that makes fibrocartilage a good shock-absorbing material, a property required for the pubic symphysis and intervertebral discs. Fibrous cartilage in the pubic symphysis has a tighter construction, reminiscent of a dense connective tissue with lacunae, whereas the structure of the intervertebral discs is more open. Fibrocartilage is also found in the menisci of the knee.

Structure and characteristics of articular cartilage

Articular cartilage demonstrates both a fluid and a solid phase, which determines its mechanical properties. The fluid phase consists of water and electrolytes and fills the gaps between the solid matrix. This fluid accounts for the majority of the wet weight of articular cartilage. The solid phase contains chondrocytes and an extracellular matrix consisting of proteoglycans, collagen fibres and non-collagenous protein. Type II collagen accounts for 90–95% of the collagen content, with the remainder made up of a variety of other collagen types.

The chondrocytes make up the cellular component and they produce and maintain the extracellular matrix. Proteoglycans account for approximately 10–15% of the cartilage structure and function to attract water, thereby improving the overall compressive strength. Proteoglycans are predominantly protein-based molecules, mostly concentrated in the middle layer and less concentrated in the deeper layers. They are made up of repeating disaccharide units (glycosaminoglycans), which are of two main types: chondroitin sulphate and keratin sulphate. Attached carboxyl and sulphate groups give the glycosaminoglycans (GAGs) a high negative charge and as a result they attract cations and water, thereby increasing the osmotic pressure of the structure.

GAGs combine with a protein core to form a proteoglycan aggrecan molecule (hydrophilic), which in turn binds to hyaluronic acid (HA) to form a proteoglycan aggregate (macromolecule), and the bond is stabilized by a link protein. The proteoglycans weave between the collagen fibres to create a solid lattice with the ability to control water movement within the structure. Water accounts for 65–80% of the articular cartilage mass, with the highest proportion being near the surface. The high water content of articular cartilage provides incompressibility properties, and when combined with its characteristic structural organization this facilitates its stress-shielding properties.

The water content reduces with ageing, leading to increased permeability, reduced strength and a reduced Young's modulus

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of elasticity. Ageing also results in increases in chondrocyte size, protein content, stiffness and keratin sulphate to chondroitin sulphate ratio, in combination with a decrease in absolute cell number and proteoglycan size. As the ageing process progresses, type X collagen is expressed, alkaline phosphatase is produced, matrix vesicles develop and matrix calcification is subsequently seen on radiographs as subchondral sclerosis.

Degradative enzymes (matrix metaloproteinases) maintain turnover of the matrix by degradation of the proteoglycan aggregates and collagen. Tissue-induced metalloproteinase inhibitors (TIMPs) regulate the matrix degradation by binding to the matrix proteins and also maintain the avascular nature of the cartilage by preventing vascular endothelial migration.

Articular cartilage provides a low friction surface that is wear resistant and the layers help to distribute weight in load-bearing joints. Articular cartilage consists of four zones and the tidemark (Figure 1 and Table 1): the zones are characterised on the basis of the chondrocyte shape and the orientation of the Type II collagen.

Metabolism, nourishment and the role of cartilage specific growth factors

Articular cartilage is avascular and relies on the diffusion of nutrients from the synovial fluid at its surface and from the subchondral bone at its deep surface. The metabolic rate is very low, with adenosine triphosphate (ATP) production *via* the lactic acid pathway. The extracellular matrix adjacent to the cellular elements has a relatively high turnover when compared to proteoglycans (weeks to months) and collagen (several years).

Various growth factors have been found to play a role in repair, proteoglycan synthesis and chondrocyte DNA synthesis. These include platelet-derived growth factor (PDGF: repair), transforming growth factor beta (TGF-*B*: proteoglycan synthesis), basic fibroblastic growth factor (b-FGF: DNA synthesis in chondrocytes) and insulin growth factor−1 (IGF-1: DNA and cartilage matrix synthesis). Parathyroid hormone and thyroxine stimulate matrix synthesis.

Mechanical properties and stress resistance

The mechanical properties of articular cartilage can exhibit great variation as result of its structural complexity and organization. Cartilage is biphasic (fluid and solid phase), visco-elastic in tension (exhibits a stress-strain relationship that is dependent on the load and the rate by which the load is applied) and anisotropic (possesses different mechanical properties depending on the direction of the applied load).

Cartilage also undergoes creep (the phenomenon of progressive deformation under constant load) and stress-relaxation (a gradual decrease in stress with time under a constant deformation or strain). These properties are made possible by movement of water and macromolecules within cartilage, as up to 70% of the water content is mobile. Whilst water has the ability to move freely, the macromolecules produce a frictional drag under high load, which restricts the flow of water and stiffens the cartilage structure. Due to the arrangement of the collagen fibres, collagen-proteoglycan relationships and cross-links, directional loading can elicit different responses depending on the direction.

In tension, the structural organization of the components is altered, resulting in increased water permeability and reduced compressive stiffness. When articular cartilage specimens are subject to a constant strain, the tensile stress-strain behaviour is non-linear. The characteristic graph curve results from an initial straightening of the slack fibres along with an increasing number of fibres being recruited. The increasing number of collagen fibrils

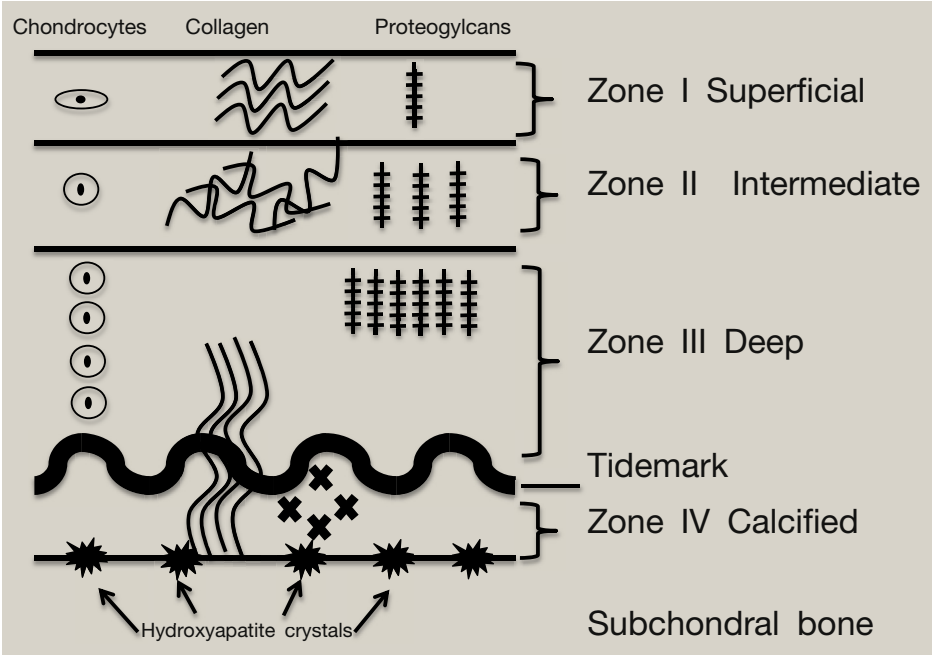

Figure 1 Zones of articular cartilage. Zone 1: Flattened chondrocytes, collagen fibres parallel to joint, sparse proteoglycans. Zone II: Round chondrocytes, oblique/random collagen fibres and plentiful proteoglycans. Zone III: Thickest layer, columns of chondrocytes, collagen bundles perpendicular to joint, cross the tidemark and are anchored into subchondral bone, highest proteoglycan content. Zone IV: Type X collagen present and hydroxyapatite crystals anchor cartilage to subchondral bone.

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