Chapter 12
Basics of the Meniscus

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Abstract The meniscus is a fibro-cartilaginous tissue located between the femoral condyles and the tibial plateau in the knee. The presence of the meniscus tissue is vital for the proper function of the knee. Meniscal injuries are very frequent cases in the orthopaedics, and they have limited self-healing capacity. The importance of the basic science of meniscus has been acknowledged for the meniscus development of regenerative strategies, and the knowledge is increasing over time. Herein, the biology, anatomy, and biochemistry of meniscus tissue are overviewed.

12.1 Introduction

The meniscus is a vital component of the knee. It is a fibro-cartilaginous tissue present between the femoral condyles and the tibial plateau. Each knee has two menisci, the lateral and medial meniscus. The meniscus has a C-like shape with a wedge-like cross-section. It is composed of different types of meniscal cells [1, 2] and the extracellular matrix (ECM) collagens fibres that are mainly the type I, proteoglycans, glycoproteins, noncollagenous and water [3, 4]. It is a complex

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tissue with a particular cell distribution [5] and specific blood supply that is important for the self-healing potential [4].

The meniscus serves certain purposes in the knee biomechanics so that the knee can function normally [6, 7]. Meniscus injuries are the most common knee injury [8] Injuries of meniscus cause pain, catching and locking in the knee. It was common to remove meniscus partially or totally in the past [4, 9]. The removal of the meniscus in the knee brings important consequences such as flattened femoral condyle, and narrowed joint space [10]. This can promote early degenerative changes in the knee [10–13]. Meniscal injuries are very frequent cases in the orthopaedics. In the clinics, treatments for the meniscus injuries depend on the patient condition and the injury [4, 14]. Due to the limited vascularity the complete self-healing of the meniscus is difficult [15, 16].

12.2 The Embryology and Development of the Meniscus

The typical crescent shape of the meniscus is achieved by the 8th–10th gestational week [17, 18]. Gray and Gardner [18] reported their observation on meniscus samples from different gestational weeks. By the gestational week 8, few collagen strands can be observed in the meniscus [18]. The condensation of the intermediate layer of mesenchymal tissue leads attachments to form towards the encircling joint capsule. Cellularity and vascularity get higher throughout the meniscus during the development. By the 9^{th} week, numerous cells, and thin strands of collagen were observed [18]. The cells located on the surface have thin and flat shape, and the cells from more deep layers appear fusiform. Blood vessels progressively get formed, and got spread almost within the entire meniscus at birth [19]. Later with a progressive decrease in the cellularity, the content of collagen increases. The collagen fibres are aligned depending on the motion of the joint and weight bearing pattern within the knee [20]. They are mainly organized in a circumferential manner. Gray and Gardner [18] reported their observation on meniscus samples from different gestational weeks. In week 10, it was observed that a Wrisberg ligament extends from the posterior portion of the lateral meniscus to the medial femoral condyle [18]. In week 12, a transverse ligament connected to the anterior parts of menisci and, a ligamentous band connects the lateral meniscus to the fibula. The meniscus is similar in week 9 and 12, only the collagen amount is higher in week 12 [18]. By week 13, the cellularity of the meniscus is higher, and the collagenous fibres were more noticeable, particularly at the horns. Another Wrisberg ligament was seen in week 14. In week 21, the collagenous fibres bundles were more ordered. In week 23, the bundles were generally parallel to each other. The appearance of the menisci at 34 and 35 weeks was similar to that of previous weeks [18].

12.3 The Gross Anatomy of the Meniscus

Lateral meniscus and medial meniscus are two smooth, shiny-surfaced whitish coloured fibro-cartilaginous tissues found between the tibial plateau and femoral condyles in each knee joint, the largest synovial joint of the human body. The menisci are crescent-shaped where the medial meniscus is less circular (Fig. 12.1), and they have a wedge-shaped cross-section with a concave top surface in accordance with the convex femoral condyles (Fig. 12.2).

The horns of the meniscus are the anchorage points to the tibial plateau. The stability of meniscus is ensured by several ligaments. Transverse ligament connects the lateral and medial meniscus from their anterior parts. The medial meniscus is attached to the tibia by its horns and merged with the knee joint capsule from its outer periphery [21]. The outer periphery of the anterior horn of the lateral meniscus enters into the tibial intercondylar eminence, and the posterior horn of the lateral meniscus continues and connects to the medial femoral condyle by the menisco-femoral ligaments [22, 23], i.e. ligaments of Wrisberg, and of Humphrey which respectively run behind and in front of posterior cruciate ligaments. Coronary ligaments are found around the menisci and enhance the attachment to the tibial plateau. However, it was reported that not all individuals have all of these ligaments [24, 25]. The medial meniscus is attached to the medial collateral ligament and thus has less ability to move. The lateral meniscus has more mobility, and it is not attached to the lateral collateral ligament. For this reason, lateral meniscus has relatively less tendency to be injured than the medial meniscus [21]. It should be

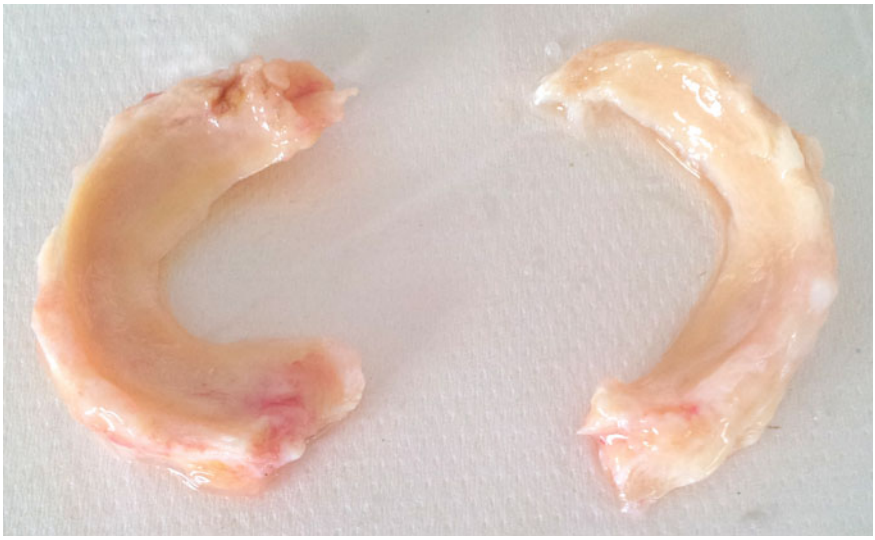

Fig. 12.1 Photographs of lateral (*left*), and medial (*right*) meniscus harvested from the right knee of a 77-years old female human donor

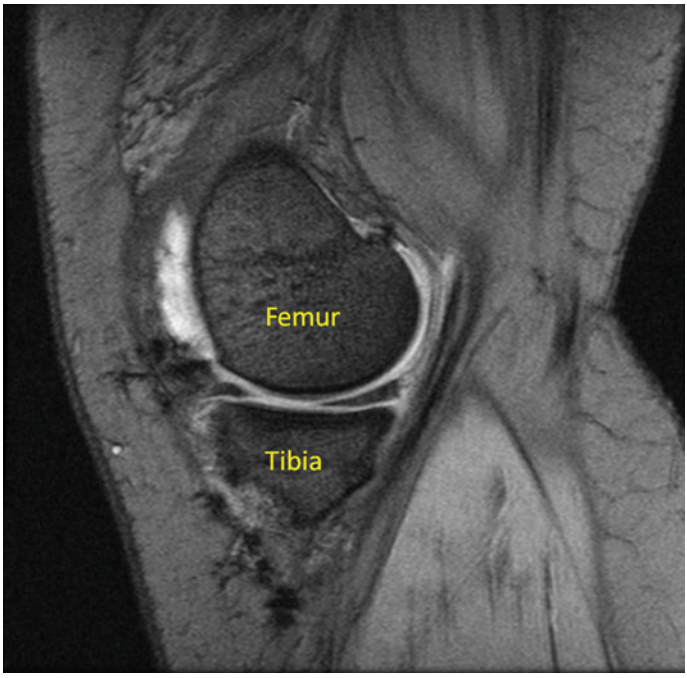

Fig. 12.2 A sagittal view from the T2-weighted MRI of the left knee of an 18-years old female subject showing the *wedge-shaped* cross-section in *black* with a *top* and *bottom* surfaces in accordance with the femoral condyle and the tibial plateau

also highlighted that while the menisci are attached to tibia and femur, they are still dynamic tissues within the knee to maintain a safe articulation [26, 27].

12.4 The Vascularity of the Meniscus

The meniscus tissue has partial blood supply limited to the outer periphery. More than a decade ago vascular anatomy of the human knee meniscus was reviewed by Gray et al. [28]. The blood vessels and lymphatics are present within the entire meniscus until the age of one. At age two, an avascular area is formed [19]. Moreover, the vascularity and lymph supply gets limited within the outer 25–33 % of the meniscus with the start of the role in load-bearing by the second decennium. The meniscus is not much exposed to biomechanical forces during the first year of the human infant. Diffusion from the synovial fluid is not enough, and direct blood supply is needed throughout the meniscus for an infant to perform standing and walking activities. With the start of the bipedal walking, the stress from the weight of the body and the muscle forces is thought to be the underlying reason of

avascularization of the inner regions [19, 28, 29]. On the other hand, the horns that have high vascularity and neural innervation, remain vascularized; this might be because they are not under weight-bearing forces [28].

The branches of the popliteal artery, i.e. medial and lateral inferior and middle geniculate arteries supply the meniscus [30, 31]. The vessels are mainly arranged in a circumferential manner with radial branches oriented to the central region of the meniscus. The perimeniscal capillary plexus extends inside the meniscus across the synovium around the meniscosynovial junction, and supplies up to one-quarter of the periphery of the meniscus. The area next to the popliteus tendon is avascular [31]. Vascular synovial tissue covers the anterior and posterior horns, and the horns receive rich blood supply [30, 31]. Endoligamentous blood vessels from the horns extend with a short-range into the bulk of the meniscus, and a direct nourishment is provided [32].

Lymphatics accompany the blood vessels throughout the meniscus. The avascular regions are nourished through the synovial fluid by diffusion or by mechanical pumping during the motion of the joint [19, 20]. And after the age fifty, the vascularity is present only within the outer 10–33 % of the meniscus [19, 28]. Therefore, while injuries in the vascular region can have the capacity to heal, the injuries where the blood supply cannot reach have limited healing capacity [28].

12.5 The Innervation of the Meniscus

The meniscus also has a role in deep sensitivity by being able to send and receive proprioceptive signals [33]. In meniscus, the nerve fibres are mostly associated with vascularity [34]. Accordingly, the nerve fibres and sensory receptors are found mainly vascular regions and get denser at the horn regions [31, 35, 36]. Like blood vessels, the neural innervation is not seen in the inner third of the meniscus [36]. The meniscus is innervated by the recurrent peroneal branch of common peroneal nerve [20, 37, 38]. The circumferential nerve fibres in the vascular region are relatively thicker while the fibres that enter radially into the meniscus are thinner. Free nerve endings, i.e. nociceptors, and three mechanoreceptors, i.e. Pacinian corpuscles, Ruffini corpuscles, and Golgi tendon organ are present in the peripheral two-thirds of the meniscus and horns [28, 34]. Pacinian corpuscles give information about acceleration and deceleration of the knee. Ruffini corpuscles provide information on the static position of the knee, the change in intra-articular pressure, and changes in the parameters of the knee motion, i.e. direction, amplitude and velocity. Golgi tendon organ acts as a protective reflex inhibitor of the motor activity of the muscles related to the knee. Nociceptors create impulses that are interpreted as pain in the brain [28].

Mine et al. [34] explained the pain sensation in the course of a fresh meniscal tear. If the tear is in the avascular region, the pain is caused by the deterioration of the micromilovia around the tear stimulating nociceptors in the synovia and the joint capsule, while in the case of a tear in the vascular region, the pain additionally

derives from the nerves within the tissue [34]. Substance P-immunofluorescent nerves are found in the knee synovial membrane and meniscus [35]. Since they have a role in pain transmission, relief of pain after meniscectomy is a commonly observed as a denervation effect [35].

12.6 The Cells of Meniscus

In what concerns cellularity, different types of cells have been observed in the meniscus, i.e. chondrocyte-like, fibroblast-like and intermediate cells [39]. However, there is no consensus regarding the classification of meniscus cells and several names such as fibrocytes, fibroblasts, meniscus cells, fibrochondrocytes, and chondrocytes are being used [40]. The outer zone cells present an oval, fusiform shape, resembling to fibroblasts in appearance and behaviour. For this reason, they may be described as fibroblast-like cells [2]. These cells display long cell extensions and are enclosed within a matrix largely composed by type I collagen, with a small percentage of glycoproteins and types III and V collagen [41]. In the inner portion of meniscus, cells have a round morphology and thus are commonly referred as fibrochondrocytes or chondrocyte-like cells [2]. These cells are embedded in a ECM consisting mainly of type II collagen, interlinked with a smaller but significant quantity of type I collagen and a higher concentration of GAGs. The outer zone cells display higher migration ability when compared to inner cells, and also seem to exhibit lower adhesion strengths [42]. A third type of cell population, with a flattened and fusiform morphology and no cell extensions, has also been identified at the superficial region of the meniscus. It has been suggested that these cells might be specific progenitor cells [43].

The phenotype and distribution of cells within the different segments and zones of meniscus has recently been investigated by Pereira et al. [44] in 44 patients. A gradual decrease of cell density from the vascular (outer) to the avascular (inner) zones was observed by histomorphometry analysis, in all the segments (i.e., anterior, middle, and posterior) of both lateral and medial menisci. Complementarily, it was found a lower cell density in the anterior sections of lateral and medial menisci when compared to the middle or posterior sections. In that work, cells with rounded and fusiform-like morphology were isolated and characterized by flow cytometry. The phenotypic analysis showed that the surface markers CD44, CD73, CD90, and CD105 were positive in more than 97 % of cells. CD31 and CD34 were being expressed in 2.3 ± 0.8 and 3.2 ± 1.0 % of cells, whereas the CD45 marker for hematopoietic stem cells was present in 0.2 ± 0.1 % of cells.

Meniscus cells isolated from vascular, avascular and mixed zone present cell plasticity and thus can be induced towards chondrogenic, adipogenic and osteogenic lineages. Outer cells also can be induced to osteogenesis lineage [45].

12.7 The Ultrastructure of the Meniscus

Meniscus composition studies have demonstrated that it possesses high water content (72 %), being the remaining 28 % portion composed by an organic component, namely ECM and asymmetrically distributed cells [15]. The ECM that surrounds meniscus cells is largely composed by several types of collagen (75 % of total organic matter). The other constituents consist in glycosaminoglycans (GAGs, 17 %) and small percentages of adhesion glycoproteins (<1 %) and elastin (<1 %) [15]. Meniscus composition differ with age, in injury or under pathological conditions [46].

Several types of collagen are present in various amounts in each meniscus segment. Type I collagen is the main type of collagen present in the vascular region (80 % dry weight), but other variants are present in small proportions (<1 %), namely type II, III, IV, VI and XVIII. In the avascular zone, collagen constitutes up to 70 % dry weight, being 60 % type II collagen and 40 % type I collagen [47].

The role of the other fibrillar component of meniscus, i.e. elastin, is not completely understood, but in adult meniscus, the combination of mature and immature fibers has been observed in very low proportions (<0.6 %) [3, 48].

Proteoglycans comprise a core protein decorated with GAGs, being their main function to enable water absorption [15]. Chondoitin-6-sulfate (60 %), dermatan sulfate (20–30 %), chondroitin-4-sulfate (10–20 %) and keratin sulfate (15 %) are the main types of GAGs present in normal human meniscus [49]. Aggrecan is the most important large proteoglycan found in meniscus tissue, while biglycan and decorin are the main small proteoglycans [50]. Also these molecules present an irregular distribution within the tissue, with a higher proportion of proteoglycans in the inner two-thirds as compared to the outer one-third.

The major adhesion glycoproteins present in human meniscus are fibronectin, thrombospondin and type VI collagen and these components serve as anchor sites between ECM and cells [51].

12.8 The Functions of the Meniscus

The meniscus has an important role on preserving knee joint stability and load transfer. Each knee has lateral and medial menisci that are attached between the tibial and femoral surfaces, thus covering two-thirds of the tibia plateau. Kurosawa et al. showed that upon total excision of meniscus, the total contact area is decreased by a third to a half in the fully extended knee [52]. Another study demonstrated the possible deleterious effects of meniscectomy in articular cartilage, subchondral bone, proximal tibia's trabecular bone and cortex [53].

The medial meniscus present reduced mobility as compared to the lateral one, due to its unique anatomy (including stronger attachment to medial collateral ligament) [54]. In a stable knee, where central pivot ligaments are functioning, the

medial meniscus has reduced involvement on anterior tibial displacement constraint. The anterior cruciate ligament impairs anterior knee motion prior to significant contact of femoral condyle with posterior horn of medial meniscus and tibial plateau [54]. Significant differences have been recognized between both femorotibial compartments on the knee joint. Lateral tibial plateau tend to have a more convex form, differing to a more concave shape on the medial compartment [54, 55]. Due to this fact, the loss of the lateral meniscus results in a significant decrease on femorotibial congruence. Additionally, most of the load transfer on the lateral compartment is supported by lateral meniscus (70 % as compared to 50 % in the medial), whereas in the medial compartment, force transmission is disseminated between articular cartilage and respective meniscus [56, 57].

The biomechanical performance of menisci to loads acting on tibiofemoral joints, results from their macro-geometry, fine architecture and insertional ligaments [55]. The collagen bundles present in the superficial layer mimic those of articular hyaline cartilage, i.e. they are randomly orientated, providing lower friction between menisci, femur and tibia during joint motion [58]. Under the superficial layer, the bulk of meniscal tissue consists in two distinct zones of collagen fibers: the inner one-third bundles that present a radial pattern, and the outer two-thirds that are circumferentially orientated. Therefore, it has been suggested that the inner third function mainly in compression, whereas the outer two-thirds may function mostly in tension. Furthermore, the bulk of meniscal tissue also presents some radially-orientated collagen fibers that act as “tie fibers”, resisting longitudinal splitting of the circumferentially-orientated collagen bundles [59].

The viscoelastic behavior of the meniscus can be correlated with its ECM composition [15]. It can be described as a rubber-like pattern at high loading frequencies, whereas at lower frequencies viscous dissipation occurs [15, 44]. This behavior is not so dependent on collagen content, but it is mainly related with GAGs and water content, i.e. higher with increasing GAGs and lower with increasing water content [60]. Segmental and zonal differences in relation to GAGs content, size and cellular density has been observed in animal meniscal tissue [61]. In a similar way to the asymmetric distribution of blood vessels and cells, the mechanical properties also differ within the different menisci [60]. Recently, Pereira et al. [44] analyzed the mechanical properties in the different segments of fresh human menisci (lateral and medial), at physiological conditions (37 °C and pH 7.4). Significant differences were observed between the medial (higher E0 and tan d) and lateral menisci. Also, when analysis was performed in combination for both menisci (medial and lateral), significant differences were observed between posterior, middle and anterior segments (posterior segments are stiffer than the middle ones, and these are significantly stiffer as compared to the anterior).

12.9 Final Remarks

The meniscus is crucial for the normal function of the knee. It is a tissue with high complexness and restricted capability for self-healing. The current treatments of meniscus lesions are not entirely satisfactory, and there is a great clinical need for appropriate tissue engineered implants. The knowledge on the biology, anatomy, and biochemistry of meniscus is expanding and is of great importance for developing improved meniscus regeneration strategies.

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