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Review

Biomaterials in search of a meniscus substitute

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ABSTRACT

The menisci fulfill key biomechanical functions in the tibiofemoral (knee) joint. Unfortunately meniscal injuries are quite common and most often treated by (partial) meniscectomy. However, some patients experience enduring symptoms, and, more importantly, it leads to an increased risk for symptomatic osteoarthritis. Over the past decades, researchers have put effort in developing a meniscal substitute able to prevent osteoarthritis and treat enduring clinical symptoms. Grossly, two categories of substitutes are observed: First, a resorbable scaffold mimicking biomechanical function which slowly degrades while tissue regeneration and organization is promoted. Second, a non resorbable, permanent implant which mimics the biomechanical function of the native meniscus. Numerous biomaterials with different (material) properties have been used in order to provide such a substitute. Nevertheless, a clinically applicable cartilage protecting material is not yet emerged. In the current review we provide an overview, and discuss, these different materials and extract recommendations regarding material properties for future developmental research.

1. Introduction

The menisci, once merely regarded as a functionless development remnant, are two semilunar fibrocartilaginous disks fulfilling key biomechanical functions in the tibiofemoral (knee) joint. Unfortunately meniscal injuries are quite common. Acute tears are most frequent in younger patients and are caused by twisting injuries [1]. Chronic degenerative tears are more frequent in elderly patients either induced by minimal twisting or stress or by chronic degenerative processes [1]. Acute symptoms encompass joint line tenderness, impaired motion (e.g. locking), and joint effusions. Whereas first documented treatments embraced swift and total meniscectomy [2], later less rigorous interventions (e.g. partial meniscectomy) were adopted after appreciating its clinical significance [3–7]. Currently, the importance of the menisci has been widely adopted and, if possible, meniscus repairs are preferentially being performed over (partial) meniscectomies [8]. However, meniscus repair techniques are not suitable for all types of tears and some patients experience enduring symptoms post meniscectomy (e.g. persisting joint line tenderness and reduced functionality) [9]. Although the development of symptomatic osteoarthritis is a complex interplay of multiple factors, it is accepted that, (partial) meniscectomy increases the risk for osteoarthritis related changes in the knee joint [10–13]. The amount of meniscal tissue removed is the strongest predictor of these chances on long term [14]. Debate remains whether degenerative osteoarthritis is more likely to follow medial or lateral meniscectomy. Some authors have reported that patients who had a lateral meniscectomy fared worse than those who had a medial meniscectomy [15–17] whereas others did not find any difference [13,18–21]. A comprehensive review suggested that, concerning partial arthroscopic procedures, there was a lower incidence of osteoarthritis following medial than lateral meniscectomy [14]. In the end, knee osteoarthritis can become symptomatic, causing knee pain, swelling, increasing disability, and reducing quality of life. [22–24] In severe symptomatic osteoarthritis, after failing non-operative treatment, only partial or total knee arthroplasty will provide marked pain relief and functional improvement [25]. However, this is a major orthopedic operation with concomitant risks and costs. Therefore, there has been increasing scientific and clinical interest

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for a meniscal substitute aimed to minimize the risk for developing knee osteoarthritis but also to offer a solution for patients suffering from enduring symptoms post meniscectomy.

Since pioneers first started, numerous materials have been used in order to produce such a substitute, from autologous tissue to synthetic materials. It is the purpose of this article to provide an overview of the different materials, and find out what recommendations can be made for future developmental research.

2. Meniscus anatomy, biochemical content and cells

The menisci are paired (one laterally, one medially) crescent-shaped pads of fibrocartilage located between the femoral condyles and the tibial plateaus, and are firmly attached via the anterior and posterior horns onto the tibial plateau (Fig. 1). The medial and lateral menisci have their own distinct anatomy, meeting anatomic constraints of the femoral and tibial condyles. The medial meniscus is firmly attached to the joint capsule and medial collateral ligament, whereas the lateral meniscus is not as rigidly attached to its circumference, mostly due to the popliteal hiatus. Although subject to anatomic variation, the anterior horns of the medial and lateral menisci are connected via the anterior intermeniscal ligament, and two more meniscofemoral ligaments connect the posterior horn of the lateral meniscus to the lateral side of the medial femoral condyle (ligaments of Humphrey and Wrisberg) [26]. Blood flow, originating from branches of the geniculate arteries, is limited to the peripheral zone whereas the central zone of the menisci receives nutrition from synovial fluid by passive diffusion [27,28]. Critically, the healing capacity of meniscal tears is directly related to its blood supply, leaving the central zone susceptible to permanent post-traumatic and degenerative lesions [28,29].

By wet weight, the meniscus is highly hydrated (72% water), with the remaining (28%) comprised of organic matter, mostly cells and extracellular matrix. Collagens make up the majority (75%) of this extracellular matrix, followed by glycosaminoglycans (17%), adhesion glycoproteins (<1%), and elastin (<1%). Collagen is the main fibrillar component of the meniscus. Different collagen types exist in varying quantities in each region of the tissue, of which type I and II are most abundant. Collagen type I appears throughout most of the menisci whereas collagen type II is mostly detected within the central part of the meniscus [30,31]. Overlap in collagen type distributions is observed throughout juvenile meniscus tissue [32] However, discrete areas with a more pronounced separation of collagen types seems to appear with increasing age [33,34]. For general comparison, type I collagen is the primary collagen in tendon tissue, and type II is the principal collagen of articular cartilage. The spatial orientation of these collagen fibers are highly functionalized in order to provide the meniscus' unique mechanical properties [35–37] (Figs. 2 and 3).

The main function of the glycosaminoglycans is to enable the meniscus to absorb water, whose confinement supports specific mechanical characteristics discussed later. The adhesion glycoproteins serve as a link between components of the extracellular matrix and cells [28].

Several types of cells can be identified within different regions of the meniscus. Within the central zone small round chondrocytes like cells (fibrochondrocytes) are mainly observed, whereas in the peripheral zone elongated fibroblasts like cells are dominant [38]. Regarding these cells and their embedding extracellular matrix, the peripheral zone of the meniscus has similarities to fibrocartilage, while the central portion demonstrates resemblance to articular cartilage [28]. Another population of cells, also known as superficial zone meniscus cells, is observed within the meniscus surface layer. These cells are believed to synthesize and secrete surface zone proteins which act as lubricant and anti-adhesive [39].

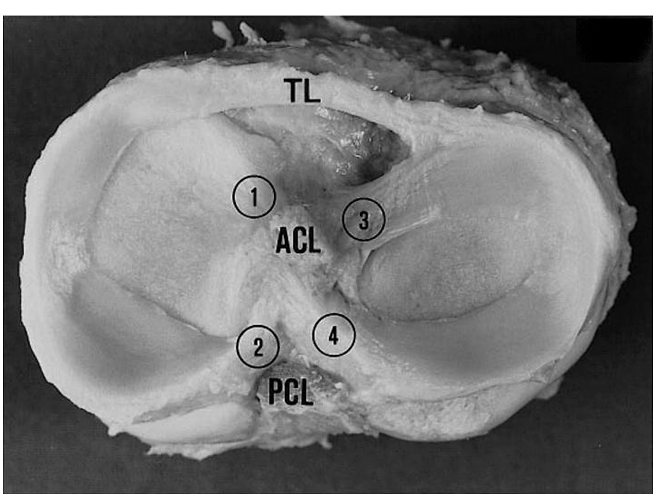

Fig. 1. Human anatomy. Right human knee joint viewed from above (the femur has been removed); the tibial tuberosity is on top. The medial (left hand side of figure) and lateral (right hand side of figure) menisci are connected by a transverse ligament. 1, anterior insertional ligament of the medial meniscus; 2, posterior insertional ligament of the medial meniscus; 3, anterior insertional ligament of the lateral meniscus; 4, posterior insertional ligament of the lateral meniscus; ACL, cross section of the anterior cruciate ligament; PCL, cross section of the posterior cruciate ligament. (reprinted from Ref. [136]).

3. Biomechanical functioning

The main function of the menisci is to transfer forces between the femoral and tibial joint surfaces, transmitting 50% through 90% of the load during weight-bearing [40,41]. Two mechanisms are mainly responsible for this load transfer [26,42]. First, the menisci transfer forces between the femoral and tibial joint surfaces by the development of hoop (circumferential) stresses within the meniscal tissue. These are tensile stresses transferred along the circumferential collagen fibers of the meniscus, counteracting the tendency of the menisci to be extruded peripherally during compressive loading. Second, as well as energy being absorbed into the collagen fibers, as the tissue is compressed energy is absorbed by the expulsion of the joint fluid out of the highly fluid absorbed menisci. An important feature of soft biological tissue is a so called stress stiffening or non linear elasticity, in which biological materials stiffen as they are strained, thereby preventing large deformations that could threaten tissue integrity [43]. This could be true also for meniscal tissue by its collagen fibers of which is mainly built up, evidenced by the different modulus at different strains in tension and compression showed in the next sections. Fiber recruitment and the braided structure of collagen fibers within the circumferential alignment may be responsible for this phenomenon.

The importance of an intact meniscus in load transfer is stressed by the increase of contact forces by 350% after meniscal loss of as little as 16–34% [44]. Even more so, radial meniscal tears extending to the periphery result in contact forces equivalent to a completely meniscectomized knee [45], which can be explained by the total disrupted hoop stress. Despite their firm attachments, menisci are dynamic structures. To effectively maintain their load-bearing function over moving, incongruent, joint surface, they have the limited ability to move as the knee flexes [46]. In Humans, following displacements in weight-bearing knees were observed (medial/lateral meniscus, mean ± SD): anterior-posterior displacement of the anterior horn 7.1 ± 2.5/9.5 ± 4.0 mm and