Cartilage Restoration, Part 1

Basic Science, Historical Perspective, Patient Evaluation, and Treatment Options

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Surgical procedures designed to treat focal chondral lesions are evolving and are supported by basic science principles of cartilage physiology and known responses to injury. Selecting the proper treatment algorithm for a particular patient depends on careful patient evaluation, including the recognition of comorbidities such as ligamentous instability, deficient menisci, or malalignment of the mechanical limb axis or extensor mechanism. These comorbidities may need to be treated in conjunction with symptomatic chondral injuries to provide a mutually beneficial effect. A central tenet of cartilage restoration is to leave future treatment options available should they become necessary. In this article (part 1), the authors review the basic science of chondral injuries, the historical perspective of the available surgical options, and present guidelines for patient evaluation and treatment.

Keywords: cartilage restoration; chondral injury; basic science; patient evaluation; treatment options; allograft; autologous chondrocyte implantation; microfracture; meniscus transplantation; mosaicplasty; osteochondral; autograft

For more than 2 centuries, the medical community has known that articular cartilage damage is a "troublesome thing and once destroyed, it is not repaired."[53] Partial-thickness articular cartilage defects do not heal but, fortunately, are only rarely associated with significant clinical problems.[75] Chondral lesions that involve the subchondral bone may fill with fibrocartilage, which has inferior biomechanical and biochemical features compared to hyaline cartilage.[16,40,75] Small full-thickness cartilage lesions can fill with fibrocartilage and render a patient asymptomatic, but large osteochondral defects are less likely to benefit from the fibrocartilaginous healing response and more frequently result in pain and disability.[30,75] Surgical procedures supported by basic science principles of cartilage physiology and known responses to injury are evolving to treat these lesions. Selecting the proper treatment algorithm for a particular patient depends on careful patient evaluation, including the recognition of comorbidities such as ligamentous instability, deficient menisci, or malalignment of the mechanical limb axis or extensor mechanism. These comorbidities may need to be treated in conjunction with symptomatic chondral injuries to provide a mutually beneficial effect. Thus, treatment of chondral injuries is often combined with ligament reconstruction, meniscus transplantation, and realignment osteotomies to achieve maximum benefit. Although cartilage restoration procedures are most commonly used to treat lesions in the knee, they are now being applied to other diarthrodial joints as well. A central tenet of cartilage restoration is to leave future treatment options available should they become necessary. In this article (part 1), we review the basic science of chondral injuries, the historical perspective of the available surgical options, and the present guidelines for patient evaluation and treatment selection. In part 2, surgical techniques and outcomes will be presented.

Incidence and Natural History of Chondral Injuries

The exact incidence of symptomatic high-grade chondral injuries is poorly defined. It has been reported that between 5% and 10% of young, active patients who present with a hemarthrosis of the knee after a specific traumatic event will have a focal chondral injury.[93] Curl et al[31] retrospectively reviewed 31 516 knee arthroscopies of patients in all age groups and reported chondral lesions in 19 827 (63%) of patients, with a mean of 2.7 articular cartilage injuries per knee. The incidence of grade III lesions was 41% and grade IV lesions was 19%. In the younger population (younger than 40 years), however, there was an incidence of unipolar grade IV lesions of the femoral condyle

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of only 5%. A review of 1000 arthroscopies by Hjelle et al[50] also reported an incidence of 5% grade III and IV chondral lesions. Many of these lesions are clinically silent at the time of detection. In a review of 993 knee arthroscopies in patients with a mean age of 35 years, there was an 11% incidence of full-thickness lesions (International Cartilage Repair Society grade III or IV)[17] that could have benefited from surgical treatment.[6] The incidence of these asymptomatic lesions in the general population can only be inferred from these limited data.

Although the precise likelihood of a lesion becoming symptomatic with time is unknown, chondral lesions have been shown to further degenerate within the knee.[67,82] In a series by Shelbourne et al, 123 incidental chondral lesions discovered at the time of more than 2700 ACL reconstructions caused patients to report lower ($P < .05$) Noyes subjective scores than did controls with normal articular cartilage after a mean of 8.7 years. Lateral chondral lesions caused worse subjective scores than did medial chondral lesions, despite the absence of changes on radiographs.[116]

Radiographic evidence of progression of untreated focal chondral defects exists, however. Recent studies following unipolar, unicompartmental full-thickness articular cartilage lesions after simple debridement have shown progression to joint space narrowing as shown on radiographs.[82] Once early changes occur on radiographs, progression toward osteoarthritis is likely.[130] Studies using newer cartilage-specific MRI protocols demonstrate a close correlation with chondral defects, clinical symptoms, and a likelihood of symptom progression.[68] After partial meniscectomy, up to 6.5% volumetric loss of articular cartilage per year has been demonstrated, implicating menisci as having a protective role.[29] Even if associated ligamentous instability is successfully treated, untreated focal chondral lesions may progress; small lesions may remain asymptomatic,[35,74] but larger lesions (>2 cm) that are not "well shouldered," meaning that the periphery of the lesion has a clearly identifiable edge with vertical walls, are likely to progress and become more symptomatic with time.[110,118]

BASIC SCIENCE

Form and Function

Articular cartilage is a viscoelastic material and therefore has variable load-bearing properties associated with different positions and activities. This vital characteristic and its role of minimizing surface friction on articular surfaces are a function of its ultrastructure composition and complex organization. Hyaline cartilage comprises an extracellular matrix that makes up approximately 95% of the tissue by volume, with sparsely distributed chondrocytes. The matrix is principally composed of type II collagen, but types V, VI, IX, X, XI, XII, and XIV are also present in smaller amounts.

Sulfated proteoglycan macromolecules constitute 12% of articular cartilage weight. Carboxyl and sulfate groups (keratin sulfate and chondroitin sulfate) on the glycosaminoglycans carry a negative charge. The negative charge creates a high affinity for water that helps cartilage resist compressive loads and causes the aggrecans to repel one another, resulting in maximal volume expansion. The flow of water through charged regions of the proteoglycan-rich matrix generates piezoelectric charges that further modulate the rate of water flow contributing to the viscoelastic behavior of articular cartilage.[124] In addition, there is evidence that electric and electromagnetic fields can produce a sustained upregulation of growth factors in articular cartilage.[1]

Chondrocytes are of mesenchymal stem cell origin and are responsible for synthesizing the matrix. In the hypoxic environment of articular cartilage, chondrocytes are mainly anaerobic. Their low turnover rate and sparse distribution allow for little cell-to-cell contact.[21] Chondrocytes constitute just 2% of the total volume of adult articular cartilage. Chondrocyte survival depends on the proper chemical and mechanical environment, including growth factors, mechanical loads, hydrostatic pressures, and piezoelectric forces.[20] Local paracrine effects have been demonstrated to drive chondrogenic processes.[70] Healthy chondrocytes are integral to articular cartilage survival, as they synthesize the extracellular matrix and contribute to the various zones of hyaline cartilage.

Each zone of hyaline cartilage has a characteristic composition and architecture consisting of chondrocytes, collagen, aggrecan, and fluid dynamics that relate directly to that zone's function (Figure 1).[21] The superficial zone consists of a "lamina splendens" layer of tightly packed collagen fibers parallel to the articular surface and a cellular layer of flattened chondrocytes. Preservation of this superficial layer is critical to protect the deeper zones. Type IX collagen is found in this layer between type II bundles that provide resistance to shear. It is thought that this layer limits passage of large molecules between synovial fluid and cartilage. The transitional layer, or intermediate zone, is composed of spherical chondrocytes, proteoglycans, and obliquely oriented collagen fibers that primarily resist compressive forces but also serve as a transition between the shearing forces on the surface and the compressive forces placed on the deeper layers. The deep zone consists of collagen fibers and chondrocytes oriented perpendicular to the articular surface, which resist compressive loads. The calcified layer consists of the tidemark that separates subchondral bone from the calcified cartilage and provides complex adhesive properties of the cartilage to bone. Collectively, these highly specialized layers produce the superior loading and minimal friction characteristics of hyaline cartilage that make it particularly difficult to restore or duplicate once it is damaged or lost. Injury to any part of this complex system can disrupt the normal biomechanical properties of articular cartilage, leading to further degeneration.

In contrast, meniscal tissue is composed of cells that are either elongated on the surface or ovoid in deeper layers. These cells are equipped with few mitochondria, suggesting anaerobic metabolism.[113] The extracellular matrix of menisci is 74% water by weight. Type I collagen composes about 65% of the dry weight, and glycosaminoglycans make up 2% of the dry weight. With this structure, the menis-

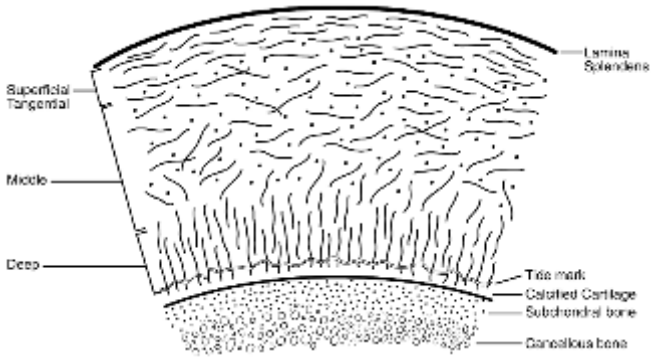

Figure 1. Diagram of articular cartilage layers, demonstrating the highly specialized composition and collagen fiber orientation of the "lamina splendens," as well as the superficial, middle, deep, and calcified cartilage layers. Superficial layers have tangentially oriented collagen fibers and resist shear, whereas deeper layers have more vertically oriented fibers to resist compression. The calcified layers (tide mark and calcified cartilage) provide complex adhesive properties of the cartilage to bone.

cus is able to resist tension, compression, and shear. Other collagens (II, III, V, and VI) make up about 5% of the dry weight. There are other noncollagenous proteins including elastin, fibronectin, and thromboplastin that probably assist in organizing the matrix by binding molecules. The blood supply to the meniscus is derived from the inferior medial and lateral geniculate arteries that form a plexus encompassing 10% to 30% the width of the medial meniscus and 10% to 25% the width of the lateral meniscus.[5] There is a 1- to 3-mm cuff of vascular synovium on the peripheral femoral and tibial surfaces. This complex blood supply is key to successful meniscal repair or transplantation. In addition, there is a network of micropores that permits synovial fluid to pump through the meniscal tissue with normal cyclical joint compression. This synovial fluid circulation is important for articular cartilage health.[87]

The structure of meniscal tissue allows it to behave as a fiber-reinforced, porous-permeable composite material containing both solid (matrix proteins) and fluid (water) components.[36,37] The function of a meniscus is to transmit load across the tibiofemoral joint, improve joint congruency, increase the surface area of joint contact, and assist in synovial fluid circulation. An intact meniscus converts joint loading forces to radial-directed hoop stresses that lead to tensile stress on circumferential collagen fibers. As a result, the menisci transmit 50% of the joint load when the knee is in extension and 90% when the knee is in flexion.[126] In vitro animal studies have demonstrated that loss of just 20% of a meniscus can lead to a 350% increase in contact forces.[113] The importance of an intact meniscus is of primary importance in the setting of articular cartilage restoration procedures. Compared to total meniscectomy, meniscal transplantation has been demonstrated to improve contact forces, thereby protecting articular cartilage, provided that the posterior and anterior horns of the meniscus transplant are adequately anchored to bone.[2,28,97]

It is well understood that the posterior horn of the medial meniscus acts as a secondary restraint to posterior-anterior translation of the tibia on the femur.[64,117] Untreated prior medial meniscectomy or incompetence of the medial posterior horn has been associated with joint instability in the anteroposterior plane, even in the setting of a properly reconstructed ACL.[115] This stability is a requirement for cartilage restoration surgery. In addition to load transmission and joint stability, an intact meniscus diminishes friction in the knee; the coefficient of friction in a meniscectomized knee is increased by at least 20%.[72] An intact meniscus disperses synovial fluid across the articular surfaces via micropores; the fluid provides chondrocytes with nutrition. The compression of the menisci with normal joint mechanics causes extrusion of the fluid out of the menisci, bathing the articular cartilage with nutrients.[87] For these reasons, it is often reasonable to consider a meniscal transplant in the setting of other articular cartilage restoration procedures in a meniscus-deficient knee.

Response to Injury

The complex structure and function of normal articular cartilage can be disrupted by even minor injuries. The response to the injury depends on the severity and depth of the injury. Low-energy, seemingly trivial superficial injuries may disrupt or damage cells and matrix and initiate a cascade toward degeneration in the absence of visible changes to the surface. Larger macrodisruption injuries may result in visible chondral fissures or partial-thickness loss. Full-thickness injuries result when the subchondral bone is violated, often resulting in an osteochondral fracture.

The highly specific microscopic anatomy and interdependent physiology of articular cartilage can be disrupted by small, superficial injuries, even without immediate cartilage loss. Superficial damage will injure chondrocytes, limit their metabolic capacity for repair, and lead to decreased proteoglycan concentration, increased hydration, and altered fibrillar organization of collagen.[71,75,77,89] Proteoglycan loss, increased water content, decreased cartilage stiffness, and increased hydraulic permeability lead to increased force transmission to the underlying subchondral bone, which increases its stiffness and, in turn, causes impact loads to be more readily transmitted to the partially damaged cartilage. This vicious cycle is thought to contribute to the progression of partial-thickness articular cartilage injuries.[88] After autologous osteochondral plug transfer, there is less stiffness of the transferred cartilage at 6 weeks, but this stiffness returns at 12 weeks.[90] The avascular nature of articular cartilage means that pure cartilage injuries do not cause hemorrhage or fibrin-clot formation or provoke an immediate inflammatory response. The chondrocytes respond by proliferating and increasing the synthesis of matrix macromolecules near the injury site, but the new matrix and proliferating cells cannot restore the surface.[75]

A full-thickness injury to articular cartilage that penetrates subchondral bone provides access to cells, blood supply, and, theoretically, a higher capacity for repair.[42]

Localized bleeding initiates a cascade beginning with hematoma formation, stem cell migration, and synthesis of type I cartilage, resulting in fibrocartilage rather than the hyaline cartilage produced by the chondrocyte.[40] This repair tissue has inferior stiffness, inferior resilience, and poorer wear characteristics than does normal hyaline or hyaline-like articular cartilage.[91] After a successful microfracture procedure (discussed in part 2), the resulting fibrocartilage covering must be protected with complete compliance with postoperative limitations to achieve optimal outcomes. Forces applied to articular cartilage restoration tissue create a challenging mechanical environment for an appropriate healing response, but studies show that without exposure to some joint motion and physiologic load, chondrocytes will atrophy.[18]

A variety of growth factors (eg, transforming growth factor–β [TGF-β], bone morphogenic proteins, insulin-like growth factor [IGF], fibroblast growth factor [FGF], and platelet-derived growth factor) influence chondrocyte and other mesenchymal cell functions such as cell migration, proliferation, matrix synthesis, and differentiation. Basic FGF (B-FGF), IGF-I, and TGF-β have been shown to stimulate matrix synthesis in vivo. Some growth factors potentiate the metabolic effects of other growth factors. For example, TGF-β can potentiate the mitogenic effects of B-FGF or IGF-I, and IGF-I and B-FGF act synergistically to increase matrix synthesis. Further work is required to identify the most effective factors or combination of factors, the optimal doses and methods of delivery, and the best methods of maintaining and releasing them at the site of cartilage injury.[23]

A thorough understanding of this complex response to injury has led to the development of gene transfer technology as novel treatment avenues for damaged articular cartilage. Several cDNAs have been cloned that could stimulate cartilage healing by inducing chondrocyte mitosis and matrix synthesis, inducing chondrogenesis by mesenchymal progenitor cells, or inhibiting cellular responses to inflammatory stimuli that damage articular cartilage. This technology is being applied to deliver a vector to a cartilage defect or through the synthesis of cartilaginous implants. The basic science behind this technology is encouraging, and in the future, perhaps it will be used to guide biological processes toward both accelerated and improved articular cartilage repair. Currently, however, there are no clinical applications to this technology available.[122]

Allograft Use and Processing

A total of 154 tissue banks were identified in a January 2001 report issued by the Office of the Inspector General Department of Health and Human Services. In the mid-1990s, the yearly number of organ donors increased more than 3-fold, from 6000 in 1994 to more than 20 000 in 1999. This remarkable increase in donor availability correlates with increases in the yearly distribution of 750 000 allografts by 1999.[33] In 1992, the most commonly distributed tissues from tissue banks were bone–patellar tendon–bone (95%), Achilles tendon (90%), fascia lata (86%), and meniscus (33%), with very little osteochondral allograft use.[123] Allograft tissue-processing techniques have been advancing rapidly over the past decade.[4,32,76,78,105,112] Data from detailed donor medical and social history and serology testing are used before graft procurement. The grafts are procured within 12 hours of death, and the tissue may be harvested with the use of sterile technique or may be procured and processed in a clean room environment. Thorough lavage removes marrow components, which are the main source of disease transmission and immune reaction. They are transferred to an antibiotic solution for a day at 37°C to kill microorganisms and subsequently stored at 4°C until used, but low temperatures may have an effect on chondrocyte viability.[128] The virucidal dose of radiation required to eliminate viral DNA is 30 kGy, which not only kills chondrocytes but also affects mechanical properties and therefore is not used for fresh osteochondral allografts.[105]

Currently, most osteochondral allografts are transplanted fresh, to preserve both cartilage cells and matrix. The success of an osteochondral graft implantation is directly related to the percentage of viable chondrocytes that remain after implantation.[128] The grafts are preserved in either lactated Ringer's solution or a physiologic culture medium to maximize the viability of the chondrocytes. Viable chondrocytes can be maintained in lactated Ringer's solution cooled to 4°C for 7 to 14 days. Recent data demonstrate a detectable decrease in the percentage of viable cells after 24 hours and a gradual decrease in chondrocyte viability at 7 days after the donor's death when grafts are stored in lactated Ringer's solution or after 14 days when grafts are stored in a physiologic culture medium.[8] After 14 days of storage, fresh human osteochondral allografts undergo significant decreases in chondrocyte viability, viable cell density, and metabolic activity. Although tissue glycosaminoglycan content and biomechanical properties of cartilage matrix are preserved during storage for 28 days, the chondrocytes necessary to maintain the matrix demonstrate decreased viability during that storage period, with the most abrupt drop occurring at 15 days.[129]

Bone marrow elements are the primary source of allograft immunogenic cells, and these are dramatically reduced during lavage at procurement. Host-donor matching of the major histocompatibility complex of chondrocyte surface antigens has further reduced the immunogenic load. Friedlaender et al[39] compared immunologic response and clinical outcome at 10 years after implantation of massive osteochondral allografts in 29 patients. In that series, 8 patients (28%) had anticlass II human leukocyte antigen responses, but of those, 5 (63%) had good to excellent results. Of the 21 without an immune reaction, 18 (86%) had satisfactory outcomes. They concluded that immune reactions found with even massive grafts were self-limited and did not preclude a satisfactory result. Since the work of Langer and Gross[61] in 1974, we have learned that although free chondrocytes are immunogenic, if the cartilage matrix remains intact, sensitization does not occur. The dense matrix in which the chondrocytes are embedded acts as a barrier that limits antigen exposure. Cartilage surface deterioration allows the chondrocytes to be

exposed, leading to sensitization. The use of immunosuppressants is another way to decrease the host response to an allograft, but it is generally thought the morbidity of this treatment greatly outweighs the potential benefit, and their use is not recommended in the setting of cartilage restoration surgery.[107]

HISTORICAL PERSPECTIVE AND BASIC SCIENCE CONSIDERATIONS OF TREATMENT OPTIONS

The first arthroscopic treatment of chondral injuries was to debride the cartilage to reduce mechanical symptoms and inflammation that may arise from inflammatory mediators. Early cartilage repair techniques penetrated the subchondral bone to recruit pluripotential mesenchymal marrow stem cells that would differentiate and form fibrocartilage.[19] Recently, autograft and allograft osteochondral plugs with true hyaline cartilage and subchondral bone have become popular. Biologic replacement with autologous chondrocyte implantation has led to more advanced biologically derived solutions to cartilage restoration. Future directions will likely involve synthetic implants and single-stage biologically active carriers or matrices.

Arthroscopic Lavage and Debridement

Efforts to debride friable inflammatory tissue began 6 decades ago when Magnusson[73] popularized this as a method of reducing mechanical symptoms. Without debridement, arthroscopic joint lavage alone provides short-term benefits in 50% to 70% of patients.[11] When combined with lavage and debridement of friable tissue, marrow stimulation appears to improve results and provide a more durable outcome.[52,56,81] Arthroscopic debridement and lavage alone have shown to have no significant lasting benefit in arthritic knees without specific localized mechanical symptoms,[86] but in carefully selected patients with a specific history of low-energy trauma, mechanical symptoms, minimal malalignment, stable ligaments, and low body mass index, arthroscopic debridement may be of some use.[49]

In 1987, Rudd et al[110] completed a canine model investigating humeral chondral defects prepared with and without beveling of the margins of focal chondral lesions at 16 weeks after defect creation. The authors identified a greater number of defects with beveled edges that progressed, compared to those created with vertical, "well-shouldered" margins. In addition, chondral damage to the glenoid surface occurred more frequently opposite beveled defects compared to those opposing defects with vertical walls.[110]

Marrow Stimulation Techniques

Soon after Magnusson described open debridement of chondral injuries, Pridie[103] described drilling of denuded areas of articular cartilage to stimulate reparative cartilage formation. In 1976, Mitchell and Shepard[85] demonstrated that such treatment resulted in repair tissue but that the early repairs deteriorated after 1 year in a rabbit model. In the early 1980s, Johnson[59] introduced abrasion arthroplasty, which used a motorized instrument to arthroscopically remove 1 to 3 mm of subchondral bone. In contrast to these techniques, the contemporary microfracture technique is a relatively reproducible and atraumatic method of exposing the defect to pluripotential marrow stem cells without bone removal or the risk of thermal necrosis. This technique, popularized by Steadman et al[119] in 1997, uses arthroscopic picks to penetrate the subchondral bone in a controlled pattern within a carefully prepared lesion. A more complete description of this technique and outcomes will be presented in part 2.

Techniques designed to stimulate marrow rely on the differentiation of primitive mesenchymal cells to produce fibrocartilage, which is repair cartilage.[26] Unlike hyaline cartilage, which contains primarily type II collagen, fibrocartilage is primarily composed of type I collagen, with marked differences in biomechanical and structural properties.[7,22] After these techniques (drilling, abrasion arthroplasty, microfracture), the extent of fill is rarely more than 75% of the total volume of the chondral defect, and the biomechanical properties of the repair fibrocartilage are inferior to those of hyaline cartilage.[23]

Cartilage Replacement Techniques

Osteochondral Autograft. Osteochondral autografts involve the transfer of intact hyaline cartilage and subchondral bone,[60] and they heal to the surrounding recipient tissue.[46] The key to this technique is chondrocyte viability because only living chondrocytes can produce and maintain the extracellular matrix of proper load-bearing capacity.[19] Osteochondral autografts are small bone plugs covered with normal hyaline articular cartilage that are removed from a relatively nonweightbearing surface and transferred in a single stage to the chondral defect. In 1985, the first results of autogenous osteochondral grafts for the treatment of osteochondritis dissecans lesions were published.[131] The first arthroscopic treatment using autografts was reported in 1993.[79] Many studies have been published since that have investigated the ideal donor site and plug size.[13,45,47,48,95] Complex contact pressures of the patellofemoral joint[41] make this a particularly challenging region with respect to osteochondral plug size, articular surface contour, and implantation technique.

Mechanical studies of autograft plugs have demonstrated that the pull-out strength of press-fit plugs using currently available systems is directly related to the length and diameter of the plug; 15-mm-long plugs had a mean pull-out of 93 N, and, of those, 11-mm-wide grafts were significantly stronger (92 N) than were 8-mm-wide grafts (41 N). These pull-out strengths were reduced by half with graft reinsertion or levering at the time of harvest.[34] In another study, fixation strength of mosaic autografts decreased 44%, from 135.7 N to 75.5 N, over a 7-day period while soaked in a physiologic solution in vitro, suggesting that there is substantial deterioration of short-term fixation strength of mosaicplasty grafts in the immediate postoperative period.[127]

In the case of graft-length mismatch, mechanical studies have demonstrated that a plug that is .5-mm proud has poorer mechanical effects and more shear than a .5-mm sunk plug. Therefore, although the mosaic bed of plugs should be constructed to match the local contour, care must be taken not to overcontour the graft construct.[25] In animal studies, grafts that were 2-mm proud demonstrated graft micromotion and fissuring, which prevented proper graft integration and function. In addition, these studies emphasized the importance of fully seating the graft in a well-supported recipient site. Supported grafts heal well, but unsupported grafts tend to subside and become covered by fibrous tissue.[99]

It is the periphery of these mosaic reconstructions that experiences the highest shear, which may lead to progression of the lesion or failure of resurfacing efforts. At the edge of prepared cartilage lesions, there is a considerable loss of chondrocytes, but these fewer number of chondrocytes are able to upgrade their metabolism to produce an equal amount of proteoglycan.[54] In the future, perhaps the combination of marrow stimulation and autologous plug transfer will provide a fibrocartilage interface for better integration between plugs and intact surrounding cartilage to reduce shear at this interface. This would conceptually integrate the strategy of reconstruction and repair, possibly providing improved histology and biomechanical stability at the periphery of the lesions after restoration.

Physiologic pressure on the donor sites is thought to be responsible for a significant amount of morbidity after autologous plug transfers. In one study, 10 of 10 donor sites' pressure films demonstrated a significant exposure to pressure with physiologic range of motion.[96] Recent cadaveric studies have shown that contact pressures are lowest along the medial trochlea and decrease distally along the lateral trochlea.[41]

The topography of various regions of articular cartilage must be taken into account when matching a donor site with a recipient lesion. Topographic mapping has demonstrated that the articular cartilage of the lateral and medial femoral trochlea matches the weightbearing portions of medial and lateral femoral condyles better than the cartilage from the central intercondylar notch does.[9]

Although originally developed to treat chondral lesions in the knee, autologous plugs are now being used with good early results to treat chondral lesions in other joints as well.[3,57] A more complete description of this technique and outcomes will be presented in part 2.

Osteochondral Allograft. Fresh osteochondral allografts provide larger constructs of subchondral bone and viable cartilage from cadaveric donors. Osteochondral allografts were first used to restore the articular surface in 1908 by Lexer,[66] who reported a 50% success rate with adequate function of the allograft and incorporation into host bone.[65] In the 1940s and 1950s, it was recognized that allografts could represent a biologic alternative to knee replacement in young patients with focal articular cartilage damage.[38] Cryopreserved osteochondral allografts were used for limb salvage after resection of bone tumors in the 1970s,[98,125] and several investigators reported moderate success rates with problems related to the massive size and limited viability of frozen chondrocytes.

Currently, osteochondral allograft implantation is contraindicated in lesions caused by diffuse disease processes, such as osteoarthritis and inflammatory arthropathies, and diffuse avascular necrosis. If avascular necrosis is localized and the surrounding bone is healthy, allograft implantation may be considered. Defects limited to one joint surface (unipolar) have better results than do lesions on opposing joint surfaces (bipolar or kissing lesions). As with other cartilage restoration procedures, an intact meniscus, ligamentous stability, and proper angular alignment of the limb are required for allograft implantation. The comorbidities of deficient or absent meniscus, ligamentous instability, and mechanical axis malalignment are treatable, however, and must be corrected before or concomitantly with allograft implantation. The upper limit of patient age for these procedures remains an area of controversy. Although the majority of investigators recommend an age limit of 40 to 45 years, others have extended this to 60 years of age in healthy, active individuals.[69,83,132]

Concerns related to frozen chondrocyte viability[108] led to the routine use of fresh osteochondral allografts when treating isolated articular cartilage defects. It is generally recommended that fresh articular cartilage allograft be transplanted within days of harvest, with the understanding that the longer the wait, the greater the death of cartilage cells. The urgent nature of using osteochondral grafts as they become available creates logistical challenges of obtaining the correct size graft at a time and place that the patient is available for surgery. Some centers have expanded the use of osteochondral allografts to include total replacement of the entire tibiotalar joint with carefully size-matched fresh cadaveric joints.[121] The technique and outcomes of osteochondral allograft implantation to treat focal chondral defects will be presented in part 2.

Periosteal and Perichondral Grafting. In the 1970s[106] and 1980s,[58] early encouraging results from perichondrium transplantations to articular cartilage defects in animals demonstrated that the transplanted tissue was histologically similar to articular cartilage with 74% type II collagen.[51,94] Only performed in a limited number of centers, this procedure works best in younger patients.[114] Because of the limited use of this procedure, there are few reported outcomes that widely endorse its use.

Biologic Techniques

Autogenous Chondrocyte Implantation. Autogenous chondrocyte implantation (ACI) is a 2-stage procedure in which an arthroscopic biopsy of normal hyaline cartilage is cultured in vitro, and the resulting chondrocytes are then reimplanted into a cartilage defect beneath an autologous periosteal patch. Animal studies began in the 1980s and led to the clinical application of this procedure after revealing the formation of hyaline-like cartilage.[15,43] In 1994, Brittberg et al[14] first reported ACI in humans, and it has grown in popularity since then.

Articular chondrocytes are embedded in the hyaline cartilage matrix, where they maintain the homeostasis of matrix proteins that are necessary for tissue matrix structure. Individual chondrocytes can be released by enzymatic digestion and expanded in culture.[44] During the expansion, the cells gradually dedifferentiate and lose type II collagen expression, but they are able to reexpress their phenotype when cultured in agarose gels.[12] Culture-expanded chondrocytes demonstrate phenotypic plasticity in their ability to form cartilage in pellet mass cultures, adipose cells in dense monolayer cultures, or a calcium-rich matrix in an osteogenic assay. In contrast with mesenchymal stem cells, chondrocytes formed cartilage only (and not bone) in the in vivo osteochondrogenic assay. These results suggest that within articular cartilage, there is a subpopulation of chondrogenic cells that exhibit a level of phenotypic plasticity that is comparable with that of mesenchymal stem cells.[120] When chondrocytes grow in culture, there is a linear relationship between their biosynthetic activity and the number of seeded chondrocytes. For this reason, the number of cells in the initial biopsy is undoubtedly important,[27] but the precise number of cells required for successful clinical implantation of the chondrocytes either as a suspension or in a scaffold has not been studied sufficiently. LeBaron and Athanasiou[62] noted that polylactide-polyglycolide scaffolds seeded with a density of <10 million cells/mL resulted in the formation of very little cartilage. They concluded that seeding at high cell density seemed desirable.[61] Puelacher et al[104] observed that seeding scaffolds at a cell density ranging from 20 to 100 million cells/mL resulted in the formation of cartilage when the scaffold was implanted subcutaneously into nude mice. In the clinical setting today, the aim is to transplant at a cell density of 30×106 cells/mL.

In the future, techniques using minimally invasive implantation will spare the patient the morbidity of an open arthrotomy. All arthroscopic techniques have been reported but are not currently implemented in the United States.[34] The all-arthroscopic technique is based on implanting a 2-mm-thick polymer fleece preloaded with autologous chondrocytes in a fibrin gel that is anchored to the condyle arthroscopically. Lee et al[63] implemented in vitro culturing of a chondrocyte-laden scaffold before implantation. In a canine model, they evaluated full-thickness focal chondral defects without bone involvement 15 weeks after implantation of an autologous articular chondrocyte–laden type II collagen scaffold that had been cultured in vitro before implantation.[63] In these cultured scaffolds, the reparative tissue formed from the scaffolds filled 88% ± 6% of the cross-sectional area of the original defect, with hyaline cartilage accounting for 42% ± 10% (range, 7%-67%) of the defect area. Further work is necessary to identify the specific culture and cell density parameters needed to maximize this advantage of in vitro scaffold culture before final implantation compared to the results of noncultured implantation.[15,100] In the future, allogenic sources of cells or single-stage biologic techniques may offer the added advantage of eliminating the need for biopsy before implantation. As ACI technology becomes more mainstream and techniques improve, it will likely be used more routinely to treat other joint surfaces as well as the knee. Recently, ACI has been used to treat shallow chondral defects in the shoulder[109] and hip (L. Peterson, J. W. A. personal communication, December 7, 2003) as well.

Meniscal Transplant. The limb-sparing reconstructions performed almost a century ago represent the first meniscal allograft transplantations that were combined with complete knee transplantation.[83] In 1989, Milachowski et al[84] performed the first isolated meniscal allograft procedure. Today, fresh meniscal allografts are custom fashioned from tibial hemi-plateaus and are implanted using arthroscopic techniques. Adequate function of the meniscal transplant relies on secure bone fixation of the anterior and posterior horns.[74,118,124] This is commonly accomplished using either bone plugs or a slot/bone bridge technique. The vast majority of menisci are transplanted into the knee to treat isolated meniscal deficiency or in conjunction with other knee abnormalities. Recently, however, the senior author (B. J. C.) used meniscal allografts in the shoulder as a biologic interposition in young patients with relatively localized articular cartilage disease of the glenohumeral joint.

DIAGNOSIS/EVALUATION

The first step in evaluating a cartilage restoration patient is to obtain a careful history, which includes the mechanism of injury, onset and pattern of symptoms, prior treatments, and the response to treatment, as well as a thorough review of previous operative reports, arthroscopic images, and videos. In one study, the average patient presenting for cartilage restoration had 2.1 previous treatments,[101] usually with a different physician. In this setting, direct verbal or written communication with the previously treating surgeons is extremely helpful.

One goal of the physical examination of a patient with chondral injury is to reveal the relative contribution of coexisting abnormalities. In addition to the sites of point tenderness, crepitus, and catching, the examination should carefully assess for the ligamentous stability of the joint, patellofemoral tracking, and the mechanical alignment of the lower extremity. In addition, the condition of the menisci and opposing articular surfaces, particularly in the symptomatic compartment, is critical. Other mechanical issues of obesity and gait patterns may exclude a patient from certain treatments because of a potential inability to comply with often extensive rehabilitation protocols.

Radiographic evaluation should include standing AP, lateral, patellar skyline (Merchant), and 45° flexion PA weightbearing views, as well as full-length alignment films. The PA weightbearing 45° flexion (skiers) view is crucial, as it brings the posterior femoral condyle into a tangential position relative to the tibial plateau. A normal-appearing joint in a standing AP radiograph may reveal severe articular cartilage damage to the posterior femoral condyle when viewed with the knee in 45° of flexion.

Recent advancements in cartilage-specific MRI technology permit precise diagnosis and measurement of articu-

lar cartilage abnormality. High-resolution fast spin echo sequence techniques can determine location, size, and depth of cartilage lesions,[102] and fat-saturation protocols combined with ionic gadolinium diethylene triamine penta-acetic acid (Gd-DTPA) contrast[24,80] can describe biomechanical and biochemical changes associated with matrix degeneration. These advancements provide preoperative information and may allow for a postoperative assessment of actual glycosaminoglycan content of repaired or replaced tissue.

Animal studies have suggested the utility of ultrasound technology in the evaluation of articular surfaces,[59] but there is no evidence of its utility in human studies. Nuclear medicine studies are not recommended to evaluate focal chondral defects of traumatic causes because of the nonspecific nature of the information they provide. In the evaluation of osteochondritis dissecans, however, a bone scan can be helpful to describe the biologic activity of the lesion fragments.

An examination under anesthesia will allow for an assessment of comorbidities that may need to be addressed. A thorough arthroscopic evaluation is valuable in determining the location, topical geography, surface area, and depth of a defect. In addition, arthroscopy allows for a formal assessment of comorbidities, such as the condition of the opposing articular surface, ligament and meniscus status, and other unsuspected cartilage defects. Grading of articular cartilage lesions depends on direct visual assessment and has interobserver and intraobserver variability. In addition to the rating systems of Outerbridge,[96] Insall,[55] Bauer and Jackson,[10] and Noyes and Stabler,[92] which are frequently cited in the literature, the International Cartilage Repair Society has offered a grading system to be used as a universal language when surgeons are communicating about cartilage lesions.[17] Verbal or written grading of articular surfaces should specify which grading system is being used and should be accompanied by a written and diagrammatic description of the lesion. Direct arthroscopic evaluation of the menisci will allow for an assessment of the quality of remaining meniscal tissue in the setting of a previous meniscectomy and aid in the decision to include a meniscal transplant in the comprehensive surgical plan.

Despite the availability of several techniques for the past 3 decades, patient evaluation and treatment selection remain challenging. This is in part owing to the fact that the natural history of commonly found asymptomatic lesions is unclear. Although it is widely believed that a symptomatic cartilage lesion is likely to persist or worsen without treatment,[67,82,116] the likelihood of a cartilage lesion detected incidentally on MRI or at arthroscopy to become symptomatic likely depends on its location, depth, geographic pattern, the demands of the patient, as well as the presence of associated comorbidities. Preexisting ligamentous instability, meniscal deficiency, or malalignment of the tibiofemoral or patellofemoral joints may cause some lesions to become more rapidly symptomatic than others. In addition, articular cartilage responds to injury with a disordered and often incomplete repair response, which adds to the highly variable pattern of symptoms seen after cartilage injury.[75,111]

TREATMENT OPTIONS OVERVIEW

Careful patient evaluation is essential in selecting the proper treatment plan. It is important to identify both the characteristics of the cartilage lesion and associated comorbidities. Untreated mechanical malalignment, ligamentous laxity, and deficient menisci are contraindications to articular cartilage restoration. Whether corrected in a staged or concomitant fashion, a comprehensive plan to address each feature of the patient's joint abnormality must be devised and discussed at length with the patient before proceeding. In the knee, ligament reconstruction, corrective osteotomies, or meniscal transplants are frequently required in addition to the articular cartilage resurfacing procedure chosen to provide a symbiosis of 2 or more mutually beneficial procedures.

It is important to avoid "linear reasoning" while evaluating a particular patient; for a specific patient at a particular point in time, there may be several viable treatment plans. A central tenet of cartilage restoration is that each treatment must allow for further treatments should they prove necessary. This paradigm of not "burning bridges" is especially important in the relatively young population, who often require more than one procedure.

We conceptualize treatment options in categories of clinical utility with considerable overlap depending on the clinical scenario (Figure 2). These categories range from those considered palliative (debridement/lavage), intended to reduce mechanical irritation and inflammatory mediators; to reparative (marrow stimulation techniques, ie, microfracture), designed to recruit pluripotential cells from marrow stromal cells to proliferate fibrocartilage repair tissue; to restorative (osteochondral grafting), designed to replace articular cartilage and subchondral bone as a single unit. Autologous chondrocyte implantation crosses the biologic boundary between reparative and restorative options. The goal of each treatment option is to provide the patient with the greatest chance for symptom reduction and a return to a productive level of function, while allowing for future treatment options, should they become necessary.

SUMMARY

The complex and highly specialized composition of normal articular cartilage makes it a formidable challenge to replace or repair once damaged or lost. Asymptomatic lesions have an unclear incidence or likelihood to progress to symptomatic defects, but after careful patient evaluation that identifies associated abnormalities, various surgical treatment options for symptomatic focal chondral defects can lead to improved function and decreased symptoms. In part 2 of this "Current Concepts" article, we will discuss the specific techniques and outcomes of these various methods of cartilage restoration.

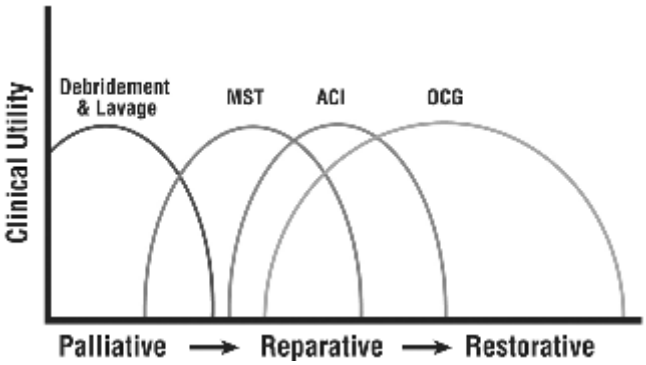

Figure 2. Overlapping treatment options ranging from palliative, to reparative, to restorative objectives, each with its own maximal clinical utility. MST, marrow stimulation; ACI, autologous chondrocyte implantation; OCG, osteochondral grafting (autograft and allograft).

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