■ TECHNIQUES IN KNEE RECONSTRUCTION

A primer in cartilage repair

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Hyaline articular cartilage has been known to be a troublesome tissue to repair once damaged. Since the introduction of autologous chondrocyte implantation (ACI) in 1994, a renewed interest in the field of cartilage repair with new repair techniques and the hope for products that are regenerative have blossomed. This article reviews the basic science structure and function of articular cartilage, and techniques that are presently available to effect repair and their expected outcomes.

Mechanical properties of articular cartilage

Articular cartilage is a hypocellular, viscoelastic tissue that lines synovial joints, providing them with a nearly frictionless environment. It is said that synovial cartilage articulations provides a coefficient of friction for joint motion that is less than one-fifth of ice on ice.¹

The mechanical properties of articular cartilage depend upon its composition and its architecture. Hyaline articular cartilage has a unique architecture (Fig. 1). The articular chondrocyte produces and maintains this matrix (Fig. 2). The surface cartilage layer, superficial tangential layer has a lamina splendens, or 'skin' that is resistant to compressive loads or penetration. The vertically arranged collagen fibers of the radial and calcified zones are resistant to shear. Proteoglycans are linked to these collagen Type II fibers by hyalonuran and link protein. Upon application of pressure to articular cartilage through weight-bearing, the water held by the highly negatively charged proteoglycans is released and exudes upon pressure. With diminished pressure, water is drawn back to the proteoglycan. A surface protein, dermatan sulfate, also acts as an anti-adhesion substance. The fine filaments of the superficial zone combine with water so that articulation with the opposite joint surface is also with combined water and superficial zone filaments.²

The lubricating barrier between joint surfaces is therefore mostly water. Water is released during weight-bearing pressure from hyper-hydrated negatively charged proteoglycans in articular cartilage. With damage or

degeneration, loss of proteoglycans and water result in impaired mechanical properties and joint function.

Incidence of cartilage lesions

The true incidence of cartilage lesions and their natural history is unknown. It has been proposed that between 5% and 10% of acute knee haemarthroses after a work-related or sports injury is associated with an acute chondral injury.³

Articular cartilage injuries are common. In a recent retrospective review of 31 516 knee arthroscopies, the prevalence of chondral lesions was 63%. However, isolated unipolar chondral defects were rare in patients under the age of 40 years. Only 5% of chondral defects were patients in this young patient population.⁴

This is clinically significant as both clinical and experimental evidence shown that with time focal cartilage injuries will enlarge and progress to osteoarthritis.⁵

Mechanical injury to articular cartilage during sporting injuries may occur with shearing forces secondary to disruption of the anterior cruciate ligament (ACL). At the time of ligament disruption, shearing osteochondral fractures may occur. Blunt injury to the joint surfaces may also cause MRI-diagnosed bone bruises. These are significant as injury and death of articular chondrocytes have been demonstrated. Arthroscopic biopsy studies of cartilage overlying bone bruises have demonstrated superficial chondrocyte death and matrix dehydration.⁶

It is proposed that cartilage cell death arises directly from the blunt trauma exceeding this threshold. Matrix breakdown occurs later as

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Fig. 1

Schematic of cartilage layers.

the chondrocyte cannot maintain the tissue homeostasis. This may account for the high incidence of osteoarthritis encountered with ACL injuries. Acutely the incidence of chondral injuries is approximately 2%, but this may approach 20% in the long run.⁷

Experimental evidence dating back to 1977 has demonstrated that even relatively low impact loads may result in chondrocyte death. In a study performed by Repo and Finlay,⁸ blunt force to articular chondrocytes in excess of 25 mPa reproducibly resulted in death of articular chondrocytes. Hence there appears to be a threshold to which articular chondrocytes can withstand blunt trauma. This may be an important factor in understanding articular cartilage degeneration after injury.

Cartilage injury, symptom development and repair

Cartilage has little intrinsic ability to heal. Absence of blood supply and endogenous source of new cells contribute to cartilage's incapacity for repair. Chondrocytes in mature articular cartilage rarely divide and their density declines with age. In contrast, lesions that extend to the subchondral marrow may heal clinically.⁹

Therefore, a cell source for cartilage regeneration or repair must arise from the underlying subchondral bone marrow, the adjacent synovial tissue or from an exogenous source. Cartilage repair is dependent on the mobilisation of cells derived from the subchondral bone marrow which include multipotential cells, osteoblasts, chondroblasts, fibroblasts, and haemato-progenitor cells.¹⁰

Fig. 2

The proteoglycans that are produced by the articular chondrocytes are highly negatively charged attracting and binding to positively charged water molecules forming a very resilient and unique visco-elastic mechanical tissue.

Articular cartilage is devoid of a nerve supply. Cartilage covers and protects the richly innervated subchondral bone plate from being stimulated. Once articular cartilage is damaged, pain can result from contact of the subchondral bone plate. If a healing response does not develop weight bearing load will be borne by the shoulders of the chondral defect. Overload and breakdown of the shoulders of the defect with a progressive enlargement of the defect may occur if several factors present in isolation or combination (Fig. 3). These include; a large defect ($> 2 \text{ cm}^2$), axial malalignment, joint instability, meniscal deficiency, activity level or a predisposition to osteoarthritis (OA). Symptoms from direct stimulation of the subchondral bone, or to the bone via an attached cartilage flap may occur. Breakdown products from the cartilage may produce synovitis which may liberate enzymes that cause effusions in the joint, capsular distention, pain, further degradation and breakdown with eventual OA. As the subchondral bone plate hardens, secondary vascular venous congestion in the medullary cavity results and may cause deep, aching pain.

Cartilage repair in the short-term may alleviate symptoms, and hopefully delay or halt the development of osteoarthritis. Thus, the goal of cartilage repair is to produce a tissue that will fill the defect, integrate with the adjacent articular cartilage and subchondral bone plate, have the same viscoelastic mechanical properties, and maintain its matrix over time without breakdown. The goal is to restore of the osteochondral functional unit with a repair tissue that approaches regeneration.

The repair tissue that results may therefore be variable dependent on the predominant cell line that proliferates and its modulation by local growth factors, cytokines, and the local mechanical environment. Small defects may benefit from debridement alone or a fibrocartilage repair that stabilises the

Fig. 3

Multiple factors influence the progression of cartilage damage to osteoarthritis. Cartilage repair may be successful in halting the progression of disease if these factors may be managed. These factors are frequently referred to as “background factors” when assessing and managing chondral defects with cartilage repair.

defect form further progression. Large defects require a better hyaline-like repair that is durable in the long run.

Surgical correction of background factors predisposing to chondral injury

Predisposing factors to chondral injury must be assessed so that these may be either corrected in a staged or concomitant fashion with cartilage repair. Otherwise treatment failure is inevitable. Tibiofemoral malalignment, patellofemoral malalignment, ligamentous, meniscal or bone insufficiency must be assessed prior to definitive cartilage repair. Long-leg alignment is assessed with long alignment digital radiographs to include hip knee and ankle for varus and valgus mechanical alignment assessment – as clinical exam is notoriously unreliable. Realignment osteotomy should correct the mechanical axis to neutral with a cartilage defect and normal joint space and overcorrect by 2° if the joint space is narrowed in order to put the cartilage repair in a favorable mechanical environment (Fig. 4).

Patellofemoral alignment is assessed by clinical examination with localisation of the tibial tubercle, the quadriceps angle measured with the patella in the reduced position in the trochlea, the presence of an active J-sign is indicative of subluxation, and the absence or presence of crepitus of the

patella with active extension of the knee indicates articular injury. A CT arthrogram performed with the knee in extension with quadriceps in the relaxed and then contracted position will assess patellofemoral subluxation and local cartilage loss.¹¹ Meniscal insufficiency is difficult to quantify with MRI scan unless the meniscus is completely absent. An arthroscopic assessment is best performed in order to assess the remaining quantity of the meniscus and the residual functional hoop stress capability.

Although arthroscopy is helpful to assess the depth and character of an osteochondral defect, a CT arthrogram is usually more useful to determine if there are subchondral bony cysts present which cannot be visualised at the time of arthroscopy.

Clinical repair for full thickness cartilage defects

The spectrum of repair tissue clinically is variable, depending on the clinical technique used, as well as intrinsic and local factors. Repair tissue may be fibrous tissue, transitional tissue, fibrocartilage, hyaline cartilage, articular cartilage, or bone, or a mixture of any of the above.

In a study conducted by Nehrer et al,¹² failed repair tissues were analysed after three techniques of marrow stimulation; drilling, abrasion, and microfracture. The repair

Fig. 4

Mechanical Axis Correction-classical mechanical axis correction for tibial valgus producing osteotomy is recommended by several authors to pass through the Kurosaka point at 62% across the width of the tibia. (Broad Green Arrow). This results in a tibiofemoral valgus angle of approximately 10 to 12 degrees. My preference is to correct the mechanical axis to the midline (red line), when correcting the varus with cartilage repair for a focal medial defect, and to only overcorrect by two degrees to the lateral tibial spine if the patient has a very large medial femoral condyle chondral defect, "kissing" medial chondral defects, or established osteoarthritis with greater than 50% loss of the joint space on weight bearing x-rays.

tissues clinically failed by 2.5 years after treatment with an average defect size $> 3 \text{ cm}^2$. Hence these techniques are recommended for smaller defects.

The techniques of arthroscopic debridement, microfracture and osteochondral graft transfer are considered first line treatment options for articular cartilage defects, predominately due to their low invasiveness. Debridement is mostly indicated for the treatment of a) incidental lesions discovered during surgery directed at other joint pathology, such as meniscectomy and ACL reconstruction; and b) lesions in lower demand patients that are reluctant to undergo other cartilage repair procedures that are more invasive and/or require long rehabilitation. Debridement is a good initial treatment option for lesions that are deemed borderline or too large for microfracture or osteochondral graft transfer. Hubbard¹³ demonstrated that in the treatment of Outerbridge grade III and IV defects, in a randomised trial of debridement against arthroscopic washout alone, debridement demonstrated measurable clinical improvement by the Lysholm score at five years in over 50% of patients, whereas this was not the case with washout which only demonstrated measurable improvement in the first year.

Arthroscopic debridement does not appear to compromise later treatment with autologous chondrocyte implantation (ACI), whereas microfracture does "burn bridges" as the failure rate of ACI after marrow stimulation is greater than three times that of ACI for debrided lesions; 26%

Fig. 5

Microfracture After release of the tourniquet bleeding is observed from the microfracture holes. A "Superclot" fills the defect, eventually forming a fibrocartilaginous repair tissue.

failure *versus* only 8%, in a study that reviewed the outcome of 330 patients undergoing ACI.¹⁴

Microfracture is a minimally invasive option whose indications have been refined in the last few years through multiple investigations. Arthroscopic curettage of damaged cartilage back to stable vertical walls and removing the calcified layer of the tide mark followed by well-spaced microfracture penetrations through the subchondral bone with a special awl are the hallmark of the procedure. A "superclot" of marrow derived cells (Fig. 5), is then carefully rehabilitated to undergo differentiation into a repair tissue. It has a high success rate when used appropriately for the treatment of small (< 2 to 4 cm^2) defects in the femoral condyles of younger (< 35 to 40 years) patients with acute defects¹⁵

Review of the clinical outcomes of microfracture overall as reported by patients in an early paper by Steadman et al,¹⁶ demonstrate that 67% reported improvement, 20% were unchanged and 13% were made worse by the procedure. 65% were able to return to strenuous sports and labor. Larger defects and those located in the patellofemoral joint deteriorate after between 24 and 36 months.¹⁷

Osteochondral autograft transfer (OAT) is generally indicated for the treatment of small (< 2 to 4 cm^2) defects in the femoral condyles and trochlea, but not the patella (Fig. 6).¹⁸

The recommendation for size is based on the limited availability of cartilage elsewhere in the knee (donor site morbidity); and to minimise the complication of plug necrosis, which is seen more frequently in central plugs that are completely surrounded by other plugs, and therefore have no direct contact to native bone for integration. Although lesions up to 4 cm^2 have been indicated for OAT, it is preferred to use this technique for active fit individuals as a first line treatment with lesions 1 to 1.5 cm^2 as it does not cause donor site symptoms in these small lesions and results in a rapid return to sport (four to eight months), with a mature hyaline cartilage repair.

Fig. 7

The technique of ACI. A periosteal patch is harvested distal to that pes anserinus tendons, it is then microsutured with interrupted 6.0 Vicryl sutures flush to the articular surface and tested for water integrity tightness. It is then sealed with fibrin glue to maintain watertightness. Finally, the autologous chondrocyte suspension is injected deep to the periosteal cover to fill the defect and the opening is sutured over and sealed with fibrin glue. The knee joint is then closed. The patient undergoes a careful rehabilitation to restore motion and allow the graft to mature uneventfully.

Autologous chondrocyte implantation (ACI) was first performed by Lars Peterson and reported in the *New England Journal of Medicine* in 1994 (Fig. 7).¹⁹

This study indicated good and excellent results in 14 of 16 patients treated on the weight bearing femoral condyles. Only two of seven patients with patellar lesions treated had similar results (maltracking was not corrected in these patients).

ACI involves a two stage technique of an arthroscopic assessment with cartilage harvest and cell cultivation followed by a second stage arthrotomy and ACI. The arthroscopy is performed to determine if the chondral defects are focal in nature and a gentle debridement to stabilise the defects, followed by a 200 mg to 300 mg biopsy of all layers of articular cartilage from a minor load bearing site (usually the lateral intercondylar notch or the superior medial margin of the trochlea). The tissue is digested and the cells cultivated, expanded and prepared for the second stage ACI under a periosteal cover as initially described by Brittberg et al,¹⁹ and presently using a collagen membrane instead, which does not undergo hypertrophy and lessens peri-operative morbidity.²⁰

The initial early indication for autologous chondrocyte implantation (ACI) was for a symptomatic full-thickness weight-bearing chondral injury of the femoral articular surface in a physiologically young patient who was compliant with the rehabilitation protocol. The results of chondral injuries for the patellofemoral joint were not as consistently high as those of the femoral weight bearing condyles initially but have improved considerably such that good and

Fig. 6

Osteochondral autograft transfer (OAT). Plug harvest from the area of the sulcus terminalis on the lateral femoral condyle is the preferred harvest site. The lateral intercondylar notch proximal to the sulcus terminalis is also a suitable site. Plug harvest from the superior lateral trochlear ridge is considered an important load bearing portion of the patellofemoral joint in 40-70 degrees of flexion and may cause significant symptoms if harvested.

excellent results can be expected in over 80% of cases when maltracking is corrected as well.²¹ This included isolated patella, isolated trochlea as well as bipolar patella-trochlea lesions. Patients with osteochondritis dissecans have also done well.²² ACI has also been effective in large chronic focal defects in the presence of early OA offering young patients an alternative to waiting for the eventuality of a total knee replacement.²³

Finally, transplanting an intact osteochondral functional unit as an allograft has been available only in University centers since the 1970s but is presently available commercially in the United States. Availability of suitable graft tissue remains the limiting factor. Fresh osteochondral allografting is associated with inherent challenges related to tissue recovery, storage, and timely delivery for treatment.

Recovery, processing, and testing of donor tissue follows guidelines established by the American Association of Tissue Banks (AATB)^{24,25} and is under the authority of the Food and Drug Administration (FDA).²⁶

Most tissue banks have a 24-hour time limit for retrieval of tissue from refrigerated cadaveric donors in a sterile operating room environment following strict sterile technique. Donors between the ages of 15 and 40 years are generally considered for inclusion in the donor pool if their articular surfaces pass direct inspection for cartilage quality.

It is policy for tissue banks to hold transplants for a minimum of 14 days to allow completion of microbiologic and serologic testing prior to release. Hence the actual surgical implantation is delayed by three and up to six weeks after

procurement, compared to the University Center clinical practice of implanting allografts usually within one week of harvest. Although results using this traditional fresh tissue protocol have been good even in mid-term follow-up²⁷ the effects of prolonged allograft storage on clinical outcomes have not yet been determined.

As per other cartilage repair procedures, the assessment of background factors and performance of concurrent procedures to optimise the mechanical environment gives the best chance for a successful outcome.

Specific conditions that are most amenable to allografting in clinical practice include osteochondritis dissecans,²⁸ osteonecrosis²⁹ and post-traumatic defects, such as those occurring after peri-articular fractures about the knee.³⁰ A particularly troublesome condition to manage is the post-traumatic tibial plateau fracture that is especially suitable to management by fresh osteochondral allograft.³¹ Allografts have also proven valuable for the salvage of knees for which other cartilage resurfacing procedures, such as microfracture, ACI, and transfer of autologous osteochondral plugs have failed.

In summary, successful cartilage repair requires a careful assessment of predisposing factors to optimise the mechanical environment for a successful repair. Equally important are the careful procedural selection based on the expected success rate of a procedure to meet patient expectations and a careful surgery and rehabilitation.

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