Cartilage Transplantation In The Knee

INTRODUCTION
Normal articular cartilage is characterized by a smooth surface with very low friction and the ability to withstand repeated high loads. Loss of this smooth surface leads to pain, loss of motion, swelling and eventually deformity. This will ultimately result in degenerative osteoarthritis.(1,2) A variety of methods have been developed over the past 20 years and are now available to regenerate cartilage and effectively reproduce its natural characteristics.

BACKGROUND
Tissue engineering to treat cartilage injury has been in use for almost 20 years. Peterson and Brittberg first described their technique of autologous cartilage implantation (ACI) in 1987. They went on to publish their first clinical results in 1994.(3) The original technique delivered the grown cartilage cells as a suspension and was contained in a piece of the patient’s own periosteum (membranous sleeve from bone). This has been refined to its current state where the cells are imbedded on to a collagen scaffold, (see Fig 5) improving the surgical technique and potentially the results.

ARTICULAR CARTILAGE AND INJURY
Articular cartilage lesions are difficult to treat in part due to the distinctive structure and remarkable function of hyaline cartilage.

Functional cartilage relies upon a homeostasis between water, chondrocytes (cartilage cells), macromolecules and type II collagen. The sparseness of cells, the unique architecture of cartilage and the fact that it is avascular, aneuric and alymphatic, give it superior loading characteristics but also the inability to spontaneously heal.(4,5)

Injury to articular cartilage is common following sporting injuries, road accidents and even accidental falls in everyday life. The injured cartilage produces a very poor healing response due to the lack of blood supply and limited inflammatory reaction, which is required for healing.

The ‘scarring’ that occurs in cartilage is inadequate and biomechanically inferior, making the surface more prone to accelerated wear and premature degenerative osteoarthritis. It would therefore seem logical to diagnose and subsequently treat articular cartilage defects early. The concepts that small lesions are insignificant is not supported and a recent study of elite soccer players demonstrated persistent knee pain due to chondral defects, even in lesions less than 10mm in diameter.(6) Pain probably occurs due to the irritation of nerve endings in subchondral bone.

Significant advances have been made in the field of prosthetic joint replacement but articular cartilage defects in younger patients (under 50 years of age), remains a problem due to the limited lifespan of these prostheses. This has led to extensive research into the knee for a biological solution for cartilage defects. There are a number of techniques which attempt to produce regeneration of native articular cartilage.

These include:
1. Microfracture  2. Osteochondral Autografts  3. Perichondral transfers  4. Allograft (cadaveric) donation 5. Autologous Chondrocyte Implantation (ACI). It is the latter technique which appears the most promising.
MAKING THE DIAGNOSIS OF A CARTILAGE LESION

As is the case in all medical conditions, a thorough evaluation of the symptomatic patient including history, examination and assessment of investigations, is the key to diagnosing chondral lesions in the knee.

Examination should document Body Mass Index (BMI), lower limb alignment, gait patterns, patellofemoral, meniscal and ligamentous evaluation, as well as signs attributable directly to cartilage lesions such as point tenderness, crepitus, catching and an effusion.

Weight bearing radiographs can demonstrate arthritic changes, but isolated cartilage lesions are best seen on high resolution MRI or under direct vision using arthroscopy.

MRI

MRI is a non-invasive tool which is becoming increasingly useful in the diagnostic assessment of cartilage defects. Newer MRI sequences are being developed to assess the biomechanical and functional profile of articular cartilage. Some sequences will potentially have the ability to assess proteoglycan content, a molecule crucial to adequate cartilage functioning.

ARTHROSCOPY

Inspection of the articular cartilage surfaces using arthroscopy may indeed be the gold standard for cartilage assessment. Despite being performed as an outpatient procedure and through “key-holes” it is still an invasive investigative tool. It does, however, allow critical assessment of cartilage surfaces as well as assessment of the rest of the knee including ligaments, menisci and global arthritic changes.

The next stage in diagnostic arthroscopy is visualization of the joint through an arthroscope the size of an 18 gauge needle so the “procedure” can be performed in the doctors office under local anaesthetic. This device is currently in use in selected units in the United States. (“Innervue” ArthroTek)

Once the diagnosis of a cartilage lesion is made (See Figure 1 and 2), clinical assessment and investigations are used to determine appropriateness for articular cartilage transplantation.

THE IDEAL PATIENT

Basic science research into the homeostasis of cartilage and increasing number of clinical reports has helped define a list of indications and contraindications for cartilage transplantation.

<table>
<thead>
<tr>
<th>Indications for ACI</th>
<th>Contraindications to ACI</th>
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<tbody>
<tr>
<td>Age &lt;55 years old</td>
<td>Inflammatory or crystal arthritis</td>
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<tr>
<td>Isolated, full thickness cartilage defect</td>
<td>Active infection</td>
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<tr>
<td>Femoral or Patellofemoral defect that is contained</td>
<td>Widespread advanced cartilage loss</td>
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<tr>
<td>Compliant rehab patient</td>
<td>Age (relative)</td>
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<td>Stable knee (Intact ligaments)</td>
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<tr>
<td>Intact meniscal cartilage</td>
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<td>Normal alignment to lower extremities</td>
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Some of these indications/contraindications can be controlled and patients can be made more “appropriate” for this surgery. For example, a malaligned knee can be corrected at the same time as the implantation of cartilage cells. Similarly, an unstable knee can have a ligament reconstruction and even a joint without a meniscus can have an artifical meniscus inserted. Age is relative, and a patient’s “physiological age” is often a more reliable indicator of surgical candidacy.
The ideal surgical candidate is often difficult to find. The ideal candidate for Anterior Cruciate Ligament reconstruction is a young, continuously active, well motivated patient with normal motion, full strength and normal biomechanics in the joint. One could argue that such a patient is too good to undergo the reconstruction. It is preferable to operate on patients without co-morbidities such as heart disease, hypertension, hypercholesterolaemia or diabetes, but this is often unavoidable and should not exclude patients with such conditions from at least consideration for operative procedures. The same is true for ACI. Even patients who are not the “ideal patient” or who have cartilage lesions that are not perfect for the procedure, should at least be assessed and ACI considered. Current recommendations suggest that patients who are perhaps borderline candidates for ACI should have as many variables adjusted (such as ligaments, alignment, and menisci) to make them more appropriate for the procedure and ultimately a better result.(8, 9, 10)

THE PROCEDURE as per the Matrix enhanced Autologous Chondrocyte Implantation (MACI) – see Figure 4

The completed process is a two stage procedure.

Stage 1 – Cell Harvest (Figure 1)

The first surgery is arthroscopic and is often undertaken to diagnose and initiate treatment for suspected lesions. At arthroscopy, once a cartilage lesion is identified (see Fig 1and 2), good cartilage cells are harvested from the non-weightbearing area of the intercondylar notch. (This is the area that is commonly cleared during cruciate ligament reconstruction.) Approximately 200 mg of cartilage cells are desired. In practical terms, this is effectively, less cartilage than a “tic-tac”. The piece of cartilage is aseptically transferred to the cartilage laboratory and the chondrocytes are extracted. Under strict highly regulated conditions the cartilage cells are multiplied in vitro, seeded on to a porcine collagen bilayer membrane and then cryopreserved. The cells can then be stored until elective re-implantation.

Stage 2 – Re-implantation (Figures 6,7 and 8)

The elective re-implantation can be performed as soon as the cells have multiplied adequately over the membrane (as soon as 4 weeks) or can be postponed until a more convenient time is available. An open arthrotomy is required for this part of the procedure. The cartilage defect is prepared to accept the graft and then the patient’s chondrocyte-seeded membrane is fixed to the defect with fibrin glue. Concomitant procedures to improve biomechanics (cruciate ligament reconstruction, patellofemoral re-alignment, osteotomy) are usually performed with this surgery. The patients can be discharged home in 1-2 days usually dependant upon the concomitant procedures.

Timing of surgery

A time lag up to one year has traditionally been offered to patients between these two cartilage implantation stages. This “wait and see how your knee goes” now seems unwise due to irreversible changes seen in the ultrastructure and durability of articular cartilage when the conforming surfaces are altered.(11) It is becoming increasingly evident that significant defects in cartilage that are left unattended cause irreversible damage to adjacent surfaces. Intuitively this seems obvious as a “pot-hole” on one side of the joint must rub and wear the opposing surface. Translating this into clinical practice, however, is difficult but implies that once a full thickness cartilage lesion is identified, cartilage transplantation should be considered as soon as practicable.

REHABILITATION

Research focused specifically on rehabilitation after MACI is currently in a rapid growth phase with new basic science studies and clinical results reported every month.

The lack of definitive research however, on the stress required to disrupt the cartilage graft has resulted in an over conservative approach to rehabilitation programmes. The past two years have seen rehab
recommendations shorten from originally 18 months to 12 months. This will shorten further as our understanding of this procedure improves.

Orthopaedic surgeons have seen a similar evolution in Anterior Cruciate Ligament (ACL) “accelerated rehab programmes”. Low shear cyclical exercise is now commenced immediately following ACL surgery resulting in faster recovery and earlier return to sport. Braces are no longer recommended and crutches are discarded by 2 weeks. We know that the ACL graft matures beyond 12 months yet appropriate rehab allows a return to cutting sports at an average of 6 months. It is an accelerated approach such as this that we can expect to see with MACI.

**Current Recommendations**

MACI rehabilitation is driven by the fact that the procedure consists of 2 stages, the initial assessment and biopsy of cartilage and finally the implantation of cultured chondrocytes through an open arthrotomy. If the second stage procedure includes a re-alignment or ligament reconstruction, this will further slow the recovery time.

The rehab also becomes specific depending on the site of the cartilage defect. A femoral condylar lesion needs to be protected from weight bearing but knee flexion is safe as long as it is undertaken in a manner to minimize shear forces. Comparatively, a patellofemoral lesion needs maximum protection from flexion/shear loads but will allow weight bearing. This means weight-bearing with the knee straight is allowed with patella lesions but stair climbing needs to be avoided in the early stage.

The rehab for cartilage transplantation has been divided into 6 stages(12)

**PHASE I:** Recovery and Protection Weeks 0-4
**PHASE II:** Inauguration Weeks 4-8
**PHASE III:** Maturation Weeks 8-12
**PHASE IV:** Integration Weeks 12-26
**PHASE V:** Functional Adaptation Weeks 26-52
**PHASE VI:** Return to Sports Weeks 26-52

(Phases V and VI are dependant on specific sporting goals.)

In brief, this means bracing and alteration in weight bearing for up to 3 months and restriction in sports from 6-12 months depending upon what the sport involves.

**RESULTS**

Fu et.al. reported over 80% of patients following ACI to femoral lesions had improvement in pain and function after 3 years follow-up.(14)

Peterson et al found 82% patients were good to excellent 5-11 years after ACI.(15)

72% good to excellent results have recently been described in elite level soccer players.(13)

This durability of ACI was found to be due to the hyaline-like cartilage repair tissue. Graft survivorship after 2 years is excellent.
COST

ACI is a newer technique and more costly than traditional conservative therapies. However, there is more in evaluating the relative merits of a surgical procedure than its dollar value. Cartilage lesions cause pain, disability and time off work. The economic burden of a cartilage defect has recently been evaluated by Lindahl et al. Assessing 57 patients over 10 years they found the cost of absenteeism and disability due to a cartilage lesion to be USD $122,807 compared to USD $5,875 for the surgery.(16)

CONCLUSION

In summary, autologous cartilage transplantation to treat articular defects in the knee is now readily available. Good to excellent clinical results are approaching 15 years. Patients need to be appropriately selected and counseled on the limitations of this technique and advised of the comprehensive rehabilitation required to ensure the success of this procedure.

REFERENCES

PICTURES

1. Intraoperative arthroscopic photo of a cartilage defect being biopsied.
2. Intraoperative arthroscopic photo of full thickness cartilage defect.
3. Arthroscopic reassessment of a fully healed defect.
4. Schematic diagram representing the stages of MACI (Matrix enhanced Autologous Chondrocyte Implantation): 1.Debridement of the lesion. 2.Culturing of the cells on to the membrane. 3.Sizing the membrane to the defect. 4.Reimplantation of the chondrocyte rich membrane.
5. Scanning Electron Micrograph demonstrating viable cartilage cells amongst the collagen fibrils of the membrane.
6. The cartilage membrane is delivered to the operating room.
7. Stage II: Operative photograph of a full thickness femoral condyle lesion.
8. Stage II: The same patient with a cartilage graft filling the defect.

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