Autologous chondrocyte implantation at the knee using a bilayer collagen membrane with bone graft

A PRELIMINARY REPORT


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Autologous chondrocyte implantation (ACI) is a technique used for the treatment of symptomatic osteochondral defects of the knee. A variation of the original periosteum membrane technique is the matrix-induced autologous chondrocyte implantation (MACI) technique. The MACI membrane consists of a porcine type-I/III collagen bilayer seeded with chondrocytes. Osteochondral defects deeper than 8 to 10 mm usually require bone grafting either before or at the time of transplantation of cartilage. We have used a variation of Peterson's ACI-periosteum sandwich technique using two MACI membranes with bone graft which avoids periosteal harvesting. The procedure is suture-free and requires less operating time and surgical exposure. We performed this MACI-sandwich technique on eight patients, five of whom were assessed at six months and one year post-operatively using the modified Cincinnati knee, the Stanmore functional rating and the visual analogue pain scores.

All patients improved within six months with further improvement at one year. The clinical outcome was good or excellent in four after six months and one year. No significant graft-associated complications were observed. Our early results of the MACI-sandwich technique are encouraging although larger medium-term studies are required before there is widespread adoption of the technique.

Autologous chondrocyte implantation (ACI) is an evolving technique, which is used for the treatment of symptomatic defects of the articular cartilage. Unlike techniques for stimulation of the bone marrow, ACI has the potential to regenerate hyaline-like cartilage.1,2 The procedure was pioneered over ten years ago for the treatment of symptomatic osteochondral defects of the knee3 and has recently been adapted for use in the shoulder and ankle.4,5

The ACI technique, as originally described by Brittberg et al,3 involved the suturing of a periosteal membrane to the rim of the debrided chondral defect. Cultured chondrocytes were then injected to fill the defect underneath the membrane. A variant of the technique uses a porcine type-II/III collagen membrane in place of the periosteal membrane.6,7 Recently, the matrix-induced autologous chondrocyte implantation (MACI) technique has been developed. The MACI membrane consists of a porcine type-II/III collagen bilayer seeded with chondrocytes. One surface has a relatively higher density of collagen fibres, giving rise to a low-friction surface which appears smooth. The other has a rough appearance because of larger gaps between collagen fibres into which chondrocytes are seeded.8 The MACI membrane can be secured directly to the base of a prepared chondral defect with fibrin glue. This technique does not require periosteal harvesting or suturing of the graft. The procedure is therefore attractive since it may be performed faster and through a less extensive exposure than conventional ACI. The MACI technique does not involve the injection of a suspension of chondrocytes below a membrane. Therefore, unlike ACI with a periosteal membrane and ACI with a collagen membrane, there is no risk of leakage of chondrocytes and uneven distribution.9 Preliminary clinical reports of the MACI technique have been encouraging.5,10 Prospective randomised studies are now under way in order to determine the efficacy of treatment.

The application of the ACI technique to deep osteochondral defects presents particular difficulties because grafts applied to defects deeper than 8 to 10 mm appear arthroscopically to undergo delayed maturation.11 One approach to the treatment of deep osteochondral defects of the knee has been to perform staged open or arthroscopic bone grafting followed four to nine months later by ACI.12,13
The clinical outcome of such a procedure has not yet been reported, but the requirement for three operative procedures after diagnosis is a significant burden to the patient. Peterson has advocated the ACI sandwich technique as an alternative. In this procedure, cancellous bone graft is used to fill the bone defect. To prevent bleeding into the cartilage defect, periosteum is sutured above the bone graft at the level of the subchondral bone plate with the cambium layer facing the joint. A further periosteal membrane is sutured to the rim of the chondral defect with the cambium layer facing the defect. After using fibrin glue to secure a watertight seal chondrocytes are injected between the membranes.

We have performed a variation of the ACI sandwich technique on eight patients using two MACI membranes rather than periosteum. We now report the technique and our early results.

**Patients and Methods**

Between April 2002 and March 2004, we performed the MACI-sandwich procedure on eight patients, five of whom were reviewed at one year after the operation.

In these five patients, the osteochondral defect resulted from osteochondritis dissecans in three, chondromalacia in one and was associated with a previously failed matrix support prosthesis in one. Four of the defects were over the medial femoral condyle and one was on the patella.

There were three men and two women with a mean age of 26.4 years (18 to 46). The mean duration of symptoms was 127 months (36 to 336). The mean size of the defect was 5.2 cm² (2.2 to 8.0). The defect was in the left knee in four patients and in the right knee in one. All the patients had undergone previous arthroscopy and the mean number of further operations was 1.6 (1 to 3). They all had pain with a median value of 5.9 on the visual analogue pain score, 10 being most severe. Other symptoms included swelling, giving-way, catching and locking.

**Operative technique.** After clinical and radiological assessment, the first stage of the procedure was arthroscopy of the knee in order to assess the site, size, depth and containment of the defect, as well as the condition of the surrounding and opposing articular cartilage. Ligamentous stability and meniscal integrity were also determined. If suitable for grafting, 200 to 300 mg of full-thickness cartilage was harvested from either the lateral or medial margin of the trochlea. The biopsy was placed in transport medium and sent to the laboratory where it was enzymatically digested, releasing the chondrocytes. After culturing of the cells for three to five weeks in serum, the patients were readmitted for the second-stage procedure.

The approach for this was through a medial or lateral parapatellar arthrotomy, using a tourniquet. The defect was excised back to a stable rim of normal cartilage. Sclerotic bone was removed from the base of the deficit with a curette. A bone window was created for harvesting of the cancellous bone graft at the distal femur immediately proximal to the medial femoral condyle. The bone window was closed and the bone graft then impacted into the base of the defect, restoring the bony contour. The stability of large defects was promoted by allowing a small volume of blood to clot among the bone graft.

The conventional MACI technique uses one membrane which is implanted with the rough side facing down, in contact with the subchondral bone. In the MACI-sandwich technique, two membranes are templated and cut to the size of the defect. Using fibrin glue (Tisseel; Baxter, Vienna, Austria), the first membrane was secured to the base of the defect with the cells facing up. The second MACI membrane was implanted on top of the first membrane with the cells facing down. The second graft was then secured with fibrin glue applied predominantly to the periphery of the graft. Light digital pressure was applied to the graft for three minutes while the glue set. The stability of the graft was then confirmed and, if necessary, supplemented by interrupted 5.0 Vicryl sutures. The wound was then closed and the leg placed in a Robert Jones bandage with a plaster of Paris backslab. Full weight-bearing was encouraged 24 hours after surgery. Once the post-operative swelling had diminished, a lightweight cylinder cast was applied for ten days with the knee in full extension. After this, the plaster was removed and an intensive rehabilitation programme began.

Clinical outcome measures included the modified Cincinnati knee scoring system, the visual analogue pain score, and the Stanmore functional rating score. Arthroscopy was performed one year after operation to assess the condition of the graft and to perform a biopsy.

**Results**

Within six months of surgery, all patients had improved modified Cincinnati knee, visual analogue pain, and Stanmore functional rating scores (Table I). There was further improvement by one year. After one year the mean modified Cincinnati knee score was 81.9, compared with 47.7 pre-operatively. Based on this score three patients had an excellent result, one a good and one a fair.
No patient developed stiffness of the knee requiring manipulation under anaesthesia, graft hypertrophy requiring unscheduled arthroscopy, or graft delamination. Four patients had arthroscopy one year after surgery. In all the grafts were stable and firm to probing. The International Cartilage Repair Society grading of the cartilage repairs was grade II (nearly normal) in two, and grade III (abnormal) in two. One graft demonstrated hypertrophy which required shaving. Diagnostic histological examination of the graft was performed in only two patients. One graft demonstrated fibrocartilage, the other mixed fibrocartilage/hyaline-like cartilage. In both, the cartilage was well integrated with the subchondral bone.

Discussion
The ACI-sandwich technique was developed for the treatment of osteochondral defects of the knee deeper than 6 to 8 mm.14 When treated by conventional ACI, restoration of the congruity of the articular cartilage is often difficult, and grafts are slow to mature.11 An advantage of the sandwich technique over staged bone grafting and subsequent ACI is that one less procedure is involved. The MACI membrane, in comparison with ACI-periosteum, reduces the operating time and surgical exposure and does not require periosteal harvesting. Such benefits make the MACI membrane particularly attractive when performing the two-membrane sandwich procedure.

Our early clinical results of the MACI-sandwich technique are encouraging and 80% of our patients had good or excellent function after one year. There were no significant complications within this period. However, the absence of pure hyaline-like cartilage in the biopsies performed after one year is of concern, but there is evidence to suggest that over time, a process of graft remodelling from fibrocartilage to hyaline cartilage occurs.18 Our findings are based on the early results of a small series. Before widespread adoption of the technique, further clarification of the medium-term clinical, arthroscopic and histological outcome of the MACI technique is required.

References