Collagen Meniscal Implant (CMI)

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6.1 Basic Science

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6.1.1 Introduction

The meniscus performs critical physiological as well as biomechanical functions within the knee. It distributes loads across adjacent articular cartilage thereby protecting the hyaline cartilage from wear. Meniscal tears are one of the most common injuries of this joint leading to the surgical excision of the injured tissue in most of the cases. However, it is well known since the pioneering works of King [1] and Fairbank [2] that the loss of meniscal tissue frequently leads to osteoarthritis and irreversible joint damage. The advent of arthroscopic partial

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meniscectomy contributed to improve these results. Nevertheless, the long-term follow-up still shows that a substantial number of patients suffered the effect of a lost meniscus [3, 4].

In an effort to keep the knee joint functional and pain free, a renewed interest in meniscal preservation techniques appeared in the last three decades. Due to the poor ability of prosthetic replacement to reproduce the meniscus behavior and the limited availability of allografts, tissue engineering techniques were developed for the same purpose. The Collagen Meniscus Implant (CMI. ReGen Biologics, Hackensack, New Jersey, USA) is a collagen based meniscus implant consisting in a resorbable scaffold designed to support ingrowths of new tissue to eventually regenerate the lost meniscus. It is a biologically resorbable implant with a spongy texture consisting of a highly purified type I collagen. The CMI was developed from bovine collagen in the early 90s in order to promote regeneration in segmental defects of meniscal tissue [5]. Stone et al. [6, 7], firstly demonstrated the ability of the implant to regenerate meniscal tissue in both dogs and humans.

To date, experimental and clinical experiences with the medial CMI have shown promising results [7–11] and a lateral implant has been developed and recently tested in several European centres.

The purpose of this chapter is to describe the CMI background and surgical technique along with some tricks and limitations gleaned from the author's experience of 15 years with its use that might help the reader to achieve the most successful outcome. The ten-year results of a medial CMI series are also presented.

6.1.2 Background

Collagen matrices, acting as templates for the growth of fibrous tissue, were developed in the early eighty's with different purposes [12–14]. Following the same investigational line, a resorbable collagen meniscus implant (CMI) was developed to support the regeneration of meniscal tissue. Experimental studies in a canine model showed that the scaffold was able to support substantial meniscal regeneration while slowly reabsorbed. In these studies, the regenerated neomeniscus had a histological and biochemical appearance that was similar to that of original canine meniscal fibrocartilage [5, 6]. Genovese et al. [15] have recently characterized the ultrastructure of the implant at a minimum of 6 moths after implantation. These biopsy findings demonstrate that host cells (likely derived from the adjacent synovium) migrate into the collagen meniscus scaffold, differentiate into fibroblast-like cells, and synthesize appropriate extracellular matrix.

6.1.3 The Implant

The CMI was conceived to conduct meniscal regeneration in the early 80s. It has physical size and shape approximating the original human meniscus. The implants are made of type I collagen fibres derived from bovine Achilles tendon. After the

tendon tissue is trimmed and minced, the type I collagen fibres are purified by using various chemical treatments to remove non-collagenous proteins and lipids. Next, the purified collagen fibres are swelled in hyaluronic acid and chondroitin sulphate and then homogenized. The swollen collagen fibres plus the glycosaminoglycans are co-precipitated by the addition of ammonium hydroxide. The precipitated fibres are dehydrated, manually oriented in a mould, lyophilized, and chemically cross-linked. Finally, terminal sterilization is performed by γ irradiation [5].

6.1.4 Patient Selection Criteria

The CMI is not a prosthetic device. It is intended to provide a resorbable scaffold that will be replaced by the patient's own tissue over time. Unlike meniscus allografts that are used to replace the entire meniscus, the CMI is designed to solely replace the damaged or missing portion of the meniscus. The ideal patient must have an intact meniscal rim and anterior and posterior horns for a good attachment and stability of the scaffold. Otherwise, would not accomplish the hoop stress law and the final construct will be extruded from the tibial plateau, resulting in a non-effective procedure. In addition, the surgically prepared site for the CMI must extend at least into the red-white zone of the meniscus to provide sufficient vascular supply.

Patients were excluded if they had had a previous treatment with collagen or if they had an allergy to collagen, inflammatory arthritis or degenerative joint disease and evidence of osteonecrosis in the targeted area. It is also contraindicated in patients allergic to bovine or other animal derived products, with an overly sensitized immune system, systemic or local infection.

6.2 Surgical Technique and Results

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6.2.1 Surgical Technique Tips and Tricks

The operative technique for implantation included an arthroscopic evaluation of the knee joint by the standard antero-lateral and antero-medial approaches. After identifying the meniscal tear, the removal of only the irreparably damaged tissue is

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performed, leaving a rim and the anterior and posterior limits square (Fig 6.1). A bleeding bed was created at the periphery by debridement into the vascular zone. If a healthy meniscal rim is achieved in the red-white zone, in order to guarantee a good vascular supply the surgeon must do a meniscal trephination (Fig 6.2). This can be performed either by passing an 18 gauge spinal needle from outside-in multiple times or conversely using a micro-fracture awl from inside-out. The created channels can also contribute for cellular in-growth. If a valgus force is applied while needling it may facilitate the partial release of the medial collateral ligament thus diminishing scuffing the articular cartilage and facilitating the whole procedure in case of medial tight knee.

The missing or removed area of the meniscus is then measured with a calibrated Teflon rod to estimate the size of the implant that was needed (Fig 6.3). The implant is prepared according to the determined defect size although over-sizing it by 3–5 mm, to get a good press fit between implant and meniscus remnant in the final construct. The implant is then inserted through the previously enlarged (about 2 cm) antero-medial or antero-lateral portal using a vascular clamp (Fig 6.4). To facilitate this manoeuvre, the surgeon stops the inflow (dry insertion) thus avoiding the flip-out of the scaffold into the joint. Then a secure attachment of the implant to the remaining host meniscus must be obtained. To this end, either an inside–out or an all-inside technique can be used. If the inside-out method is to be used, a complete set of zone specific cannulae as well as an additional posterior approach or several small stab wounds to retrieve the suturing needles are necessary (Fig 6.5). As for any meniscal repair, 2.0 non-absorbable sutures are recommended. Vertical mattress sutures all along the meniscus rim and horizontal sutures at the anterior and posterior ends of the implant were preferred (Fig 6.6) The stitches were placed every 5 mm apart and tied directly over the posterior part of the medial or lateral aspect of the capsule, depending on the meniscus to be

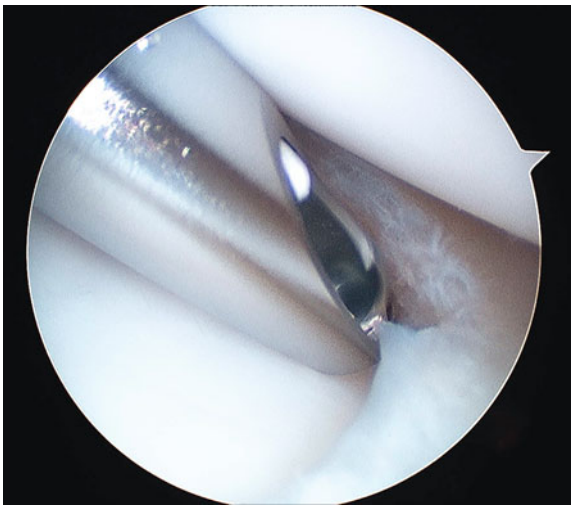

Fig. 6.1 Meticulous preparation of the implant bed with removal of damaged tissue to guarantee a stable rim in which the implant can be properly fixed

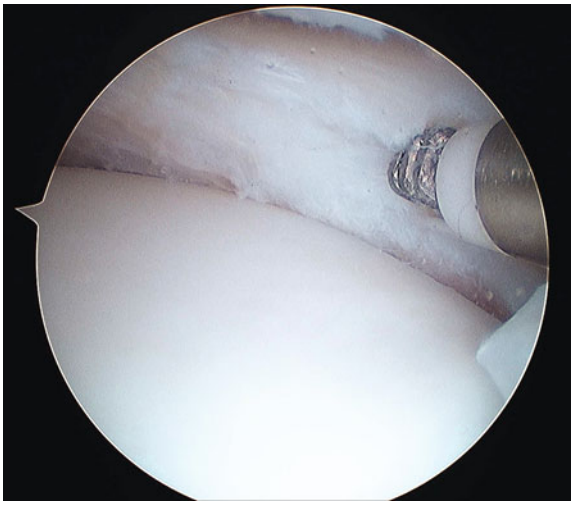

Fig. 6.2 High frequency trephination of the synovial and meniscal bed in order to guarantee a vascular supply. Note the anterior limit of the meniscal defect trimmed square

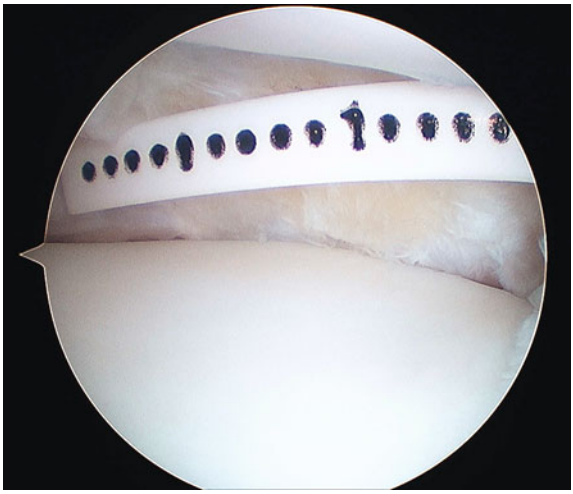

Fig. 6.3 A calibrated Teflon rod is used to measure the dimension of the defect and thus the size of the implant to be used

repaired [16]. However, if the surgeon uses an all-inside suture system (i.e. Fastfix, S&N, Andover, USA) more room between the stitches, about 1 cm, seems to be also adequate.

6.2.2 Especial Situations

Knee instability or axial malalignment in the lower extremity are common associated problems. ACL reconstruction can be performed concurrently with the CMI implantation. In that case, the tunnels for the ACL reconstruction are drilled first

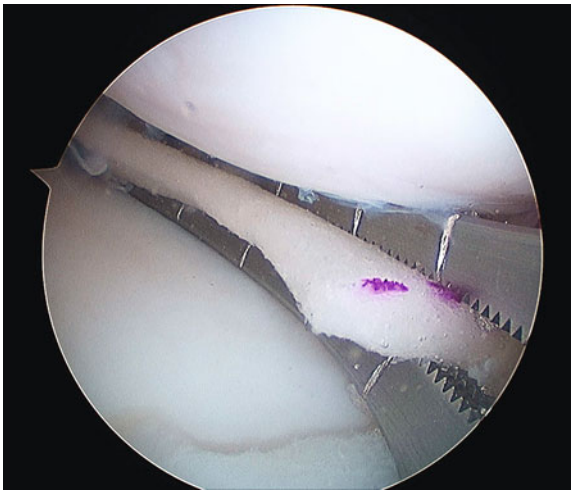

Fig. 6.4 Dry insertion of the CMI using a *vascular clamp*

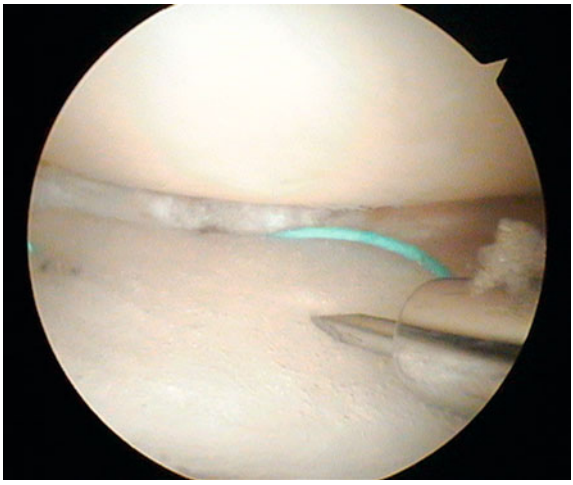

Fig. 6.5 Inside-out suture using zone specific cannulae

and the graft is passed and secured at the femoral site. Then the surgeon proceeds with the meniscal implant avoiding any over tension in the involved compartment. Once the implant has been correctly secured the knee is drawn to 20° of flexion and the ACL graft fixed at the tibial site.

If the procedures are to be staged, the CMI implantation typically should be performed first. The ACL reconstruction should be completed within 12 weeks after CMI implantation since knee instability is detrimental to the implant as noted.

If there is axial malalignment of the lower extremity, it should be corrected before or at least concurrently with the placement of the implant. Malalignment may excessively overload the involved compartment, possibly resulting in damage

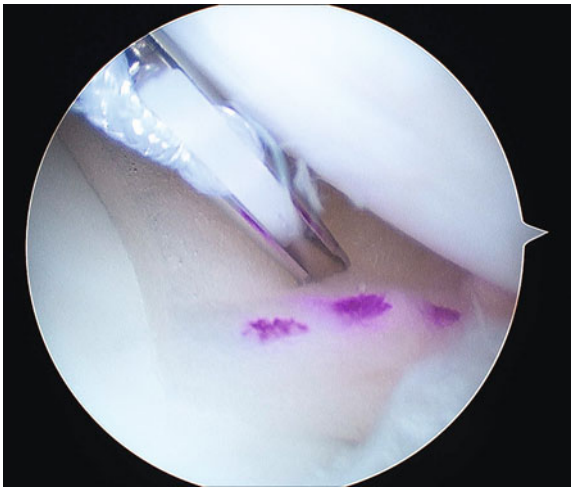

Fig. 6.6 The all-inside suturing system used at the anterior end of the implant

to the implant during the early regenerative process. No controlled studies have been conducted to confirm this possibility. Whether or not there is a coexisting OA with the malalignment, consideration should be given to correcting those abnormalities prior to or at least concurrent with the CMI implantation.

If the osteotomy and the implant procedures are done concurrently, consideration must be given to the CMI-specific rehabilitation program.

6.2.3 Rehabilitation

The rehabilitation protocol was defined as follows: patients had to wear a knee brace locked at full extension and were non-weight bearing for the initial 2 weeks while using crutches to walk. The brace could be removed to perform passive range of motion (ROM) exercises. After 4 week, the brace was discontinued for unlimited active and passive ROM exercises and patients increased weight bearing up to full weight bearing by the 6th week. After 8 weeks, patients discontinued the use of crutches. Strengthening exercises progressed from right after surgery until patients returned to full unrestricted activity. Return to sports was not recommended earlier than 6 months after CMI implantation.

6.2.4 Results

Several clinical non-randomized follow-ups have studied the collagen based implant and observed a re-growth of meniscal-like tissue and improvement of knee function overtime in a significant number of cases. Zaffagnini et al. prospectively evaluated the results of a short series of 8 patients after CMI implantation at a

follow up of 6–8 years. All patients were able to return to daily activities without limitations 3 months after surgery. Both the subjective Cinncinatti Knee Rating Scale and objective IKDC scores showed improvement in all but one case. The patient had sustained an ACL re-injury. MRI showed an altered signal in five cases and a normal signal in two. In this series, a reduction in the implants expected size was a common finding.

Bulgheroni et al. have also investigated the medial CMI in a series of 34 patients with radiological and magnetic resonance imaging. Lysholm and Tegner activity scores at 2–5 years after surgery improved significantly compared to the preoperative scores. The MRI signal also improved over time after implantation. There was a progressive decrease in signal intensity but it was not comparable to the signal of a normal meniscus. The chondral surfaces of the medial compartment had not degenerated further since placement of the CMI. If compared to a normal medial meniscus, the CMI-new tissue complex had a slight reduction in size in most cases.

Monllau et al. followed-up 25 patients who underwent arthroscopic implantation of the collagen meniscus device. Indications were persistent compartmental joint line pain due to a previous medial meniscus resection (5 cases) or a large irreparable meniscus tear found at arthroscopy (20 cases). It was possible to evaluate 22 patients at a minimum of 10 years after the procedure. The improvement of clinical functional scales and pain was considered highly significant at 1 year follow-up and the results have remained unchanged over time. Radiographic evaluation showed either minimal or no narrowing of the joint line at the most recent follow-up. According to the Genovese criteria [15], magnetic resonance imaging showed meniscus type 2 in two-thirds of the cases. Again, all cases showed a new meniscus of less volume than expected. The failure rate in the patient population was 8 % (2 of 25). There were no complications related to the device.

Recently, Zaffagnini et al. [17] analyzed a series of 33 patients with meniscal injuries at 5–10 years after surgery. Some of the patients were non-randomly treated with a medial CMI while the rest (matched controls) were treated with partial meniscectomy. The CMI group showed a significantly lower VAS for pain, and a higher objective IKDC, Tegner index and SF-36 scores when compared with the partial meniscectomy group. Radiographic evaluation also showed significantly less medial joint space narrowing in the CMI group. The MRI evaluation of the CMI patients revealed 11 cases of myxoid degeneration signal. Therefore, in this series the CMI treatment seems to be superior to meniscectomy in terms of pain, activity level, and radiological outcomes at a minimum 10-year follow-up when compared with partial meniscectomy alone.

This information was further refined by the large study conducted by Rodkey et al. [18]. These authors published a prospective multicenter randomized controlled trial comparing medial CMI with partial medial meniscectomy at an average of 5 years follow-up. Three hundred and eleven patients with meniscal problems were divided into two study arms. One group was considered acute, meaning patients without previous surgery to the involved meniscus. The second

group was chronic, those patients having had one or more prior meniscectomies. They were randomly assigned either to receive a collagen meniscus implant or to have a partial meniscectomy. Patients receiving a CMI agreed to have a second look arthroscopy at one-year after implantation to assess the amount and quality of the new tissue growth. According to the Tegner score, chronic patients receiving an implant regained significantly more of their lost activity than did controls and they had significantly fewer reoperations in the involved knee. However, no differences were detected between the two treatments in acute patients. On the other hand second-look arthroscopies performed 1 year after implantation demonstrated that the CMI supports the formation of a new biomechanically competent meniscus-like tissue.

6.3 Summary

According to the available literature, meniscal substitution with the CMI provides significant pain relief and functional improvement after a minimum of 10 years' follow-up. The implant generally diminished in size, but the procedure proved to be safe and had a low rate of implant failure on a long-term basis. No development or progression of degenerative knee joint disease was observed in most cases. The most benefit seems to appear in symptomatic patients with a previous meniscectomy, particularly when the implantation is compared with a new iterative meniscectomy.

Although the CMI is safe for the joint and had no apparent negative effects, the efficacy of this device in reducing the risk of degenerative disease remains to be proven.

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