Clinical Application of Scaffolds for Partial Meniscus Replacement

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Meniscal tears are common injuries often treated by partial meniscectomy. This may result in altered joint contact mechanics which in turn may lead to worsening symptoms and an increased risk of osteoarthritis. Meniscal scaffolds have been proposed as a treatment option aimed at reducing symptoms while also potentially reducing progression of degenerative change. There are two scaffolds available for clinical use at the present time; Collagen Meniscus Implant (CMI) (Ivy Sports Medicine, Gräfelfing, Germany) and Actifit (Orteq Sports Medicine, London, UK). Medium-long term data (4.9 to 11.3 years) demonstrates efficacy of partial meniscus replacement. The patients that seem to benefit most are chronic post meniscectomy rather than acute meniscal injuries. Herein we report on available clinical data for CMI and Actifit while describing our preferred surgical technique and post-operative rehabilitation programme.

Keywords: “meniscal scaffold”, “meniscal substitution”, “knee”, “partial meniscectomy”

INTRODUCTION

Meniscal tears are the most common type of knee injury, with an incidence of meniscal injury resulting in meniscectomy of 61 per 100 000 population per year [1] The menisci have been found to play a vital role in distributing load, delivering congruency, enhancing stability, and contributing to lubrication and nutrition [2, 3] Any substantial loss of meniscal tissue after a meniscectomy can permanently alter the biomechanical and biological environment of the joint [4] This results in increased contact stresses directly proportional to the amount of meniscal tissue removed, with a total removal of the menisci resulting in a 200% to 300% peak contact stress increase [5, 6] These increased intra-articular contact stresses within the knee after meniscectomy are associated with biochemical changes, including loss and disaggregation of proteoglycan, an increase in synthesis of proteoglycan and an increase in hydration [7] The outcome is the development of osteoarthritis. This association was first established by Fairbank in 1948 [8]. Roos et al [9] also demonstrated a relative

risk of 14 for osteoarthritis of the knee at 21 years after meniscectomy. It therefore appears important to preserve as much meniscus as possible in the event of injury. Ideally this should be by way of repair, however meniscal allograft transplantation appears to be a suitable option in cases of total meniscectomy [10-13] When partial medial meniscectomy is performed where the peripheral meniscal rim is intact and there is sufficient anterior and posterior horn tissue present for attachment, meniscal scaffolds can be used to fill the defects so as to help regenerate host tissue. There are two commercially available scaffold options for reconstruction: Collagen Meniscus Implant (CMI) (Ivy Sports Medicine, Gräfelfing, Germany) and Actifit (Orteq Sports Medicine, London, UK). This review will describe the current evidence for use of both scaffolds as well as our surgical technique.

COLLAGEN MENISCAL IMPLANT

CMI (formerly known as Menaflex) is a porous collagen-glycosaminoglycan (GAG) matrix. CMI is composed of purified type I collagen isolated from bovine Achilles tendons. The remaining portion of the CMI consists of GAGs including chondroitin sulfate and hyaluronic acid. It is chemically cross-linked with formaldehyde and sterilized using gamma radiation. There were numerous in vitro and in vivo animal studies performed which showed that the scaffold would support new tissue ingrowth as it is resorbed or assimilated into the new tissue over time[14-16]

Histological findings from an initial phase-I clinical feasibility study showed that between 3 and 6 months post-surgery the CMI was gradually replaced with immature collagen [16] Using electron microscopy, Reguzzoni et al. [17] also further defined regeneration by observing parallel lacunae walls with collagen fibrils, blood vessels, and fibroblast-like cells at 6 months following posterior horn CMI use in 4 subjects. No inflammatory cells were detected. In a phase-II clinical feasibility study by Rodkey et al. [18] results of 8 CMI patients with a 2-year follow-up validated the ability of CMI to support the regeneration of a new tissue and to improve symptoms in patients.

In the same cohort of patients Steadman et al. [19] then reported on mid-term follow up at a mean of 5.8 years. Mean Lysholm and Tegner Activity Scores were significantly improved. MRI evaluation demonstrated no degeneration in the chondral surfaces. There were no remnants of the collagen meniscus implant observed with fibrocartilage and organized extracellular matrix in all 3 of the patients that were biopsied without evidence of infection, inflammation, or immune reaction. On second look arthroscopy an estimation of meniscal defect fill was reported as 69%. Further mid-term results of the CMI procedure in 8 patients were published by Zaffagnini et al. [20] at 6 to 8 years' follow-up. They observed that although the implant generally diminished in size, the outcome was highly satisfactory and the implant may have a chondroprotective effect

Those small number studies were then followed by the only prospective multicentric randomized clinical trial by Rodkey et al.[21] comparing clinical results of the collagen meniscus implant with partial meniscectomy at 4.9 years follow-up in 311 patients. The patients were divided into an acute group with no prior surgery to the medial meniscus and a chronic group with previous surgery to the involved meniscus. The patients were randomized either to undergo CMI treatment or partial medial meniscectomy (control group). Second-look arthroscopies showed that the CMI had resulted in a significant increase in total tissue surface area and biopsies performed at 1 year postoperatively showed that the implant was able to provide a scaffold for the formation of meniscus-like fibrochondrocytic matrix by the host. The patients in the chronic CMI group regained significantly more of their lost activity than did the chronic control patients. However, comparison of the 2 acute groups showed no difference in clinical outcomes. The risk of a reoperation in the patients who had had a partial meniscectomy only was 2.7 times greater than that for the patients who had received a collagen meniscus implant.

Bulgheroni et al [22] showed further mid-term results in 28 patients receiving CMI implants. Lysholm and Tegner scores showed significant improvement and were unchanged between 2 and 5 years post-surgery. Radiographic evaluation showed no deterioration of the implant at 5 years and although MRI signal intensity was still abnormal at 5 years it had progressively decreased between 2 and 5 years.

A longer term outcome study with minimum 10 year follow up by Zaffagnini et al [23] showed that CMI provides statistically significantly improved clinical and radiological outcomes compared with partial medial meniscectomy. The VAS for pain, objective IKDC, Tegner index, and SF-36 scores confirmed this difference. Radiographic assessment showed significantly less medial joint space narrowing in the CMI group. However, a progressive CMI signal maturation over time was not observed with only 24% having normal signal on MRI evaluation. In the only other long term study Monllau et al [24] demonstrated significant improvement in Lysholm and VAS pain scores without development or progression of degenerative knee disease in most patients at a minimum follow-up of 10 years. The MRI evaluation again showed only 21% of implants had normal signal, with a decrease in size of all implants over the study period.

A recent short term study [25] looked specifically at CMI use on the lateral side which had not been studied before in depth. They reported significant improvement on all clinical scores (Lysholm, Tegner, IKDC, VAS pain score) at 2 years in 24 patients. On MRI evaluation 3 cases (12.5%) showed the CMI was the same size as a normal meniscus with 12 cases (75%) reduced in size and 3 cases (12.5%) being completely resorbed. In 9 cases (37.5%) the MRI signal was comparable to normal meniscus. Another recent short term study [26] confirmed improvement in the same clinical scores in 12 patients at one year follow up. (Table 1)

ACTIFIT

The Actifit meniscal implant (Orteq Sports Medicine, London, UK) is a novel, slowly biodegradable, synthetic, acellular scaffold composed of aliphatic polyurethane. The polyurethane is composed of 2 segments; polycaprolactone and urethane. The polycaprolactone segment degrades first by hydrolysis of the ester bonds within it. This process takes up to 5 years [27]. The urethane segments are more stable and are phagocytized by macrophages or giant cells or become integrated into the surrounding tissue over a longer period [28, 29]. It is a highly porous structure (approximately 80%) and along

147 with the degradation characteristics, the period of stability is maintained long enough to provide
148 satisfactory function while the host tissue infiltrates the porous structure [30, 31]
149
150 Initially preclinical canine studies showed scaffold integration with the peripheral capsule and
151 complete infiltration of all pores of the implant with vascularized fibrous tissue, without causing a
152 foreign body reaction [32-36] The first clinical study published by Verdonk et al [37] included 52
153 patients who had polyurethane scaffolds implanted post partial meniscectomy. Dynamic contrast
154 enhanced MRI at 3 months revealed 81.4% had tissue ingrowth. Scaffold biopsies were taken at 12
155 months in 44 patients which showed vital tissue in all samples with a tri-layered organization. The
156 cartilage status was assessed with standard MRI and second look arthroscopy and proved to remain
157 stable over the period of the study. In the same group of patients at 2 years follow-up there was a
158 statistically significant improvement in all clinical outcome scores including KOOS, Lysholm, VAS
159 and IKDC. Only one case required scaffold removal due to non-integration, although the patient was
160 asymptomatic [38]
161
162 Efe et al [39] implanted 10 patients with PU meniscal scaffold and showed a statistically significant
163 improvement in KOOS and Knee Society Score at 12 months of follow-up. MRI also showed a stable
164 scaffold appearance and a preserved articular cartilage status. A study from the same unit; including a
165 further 8 patients; again showed improvements in all patient reported outcome scores compared to pre
166 operative levels at 2 years [40]. In one case there was complete resorption occurring between 12 and
167 24 months. There was also one case of complete scaffold extrusion with 3 cases of partial extrusion,
168 although this didn't appear to affect clinical outcomes; a finding consistent with previous reports [41,
169 42].

170 Spencer et al [43] reported on 23 patients with both CMI (12 patients) and polyurethane meniscus
171 scaffold (11 cases). Overall clinical outcome at a mean of 19.1 months of follow-up was satisfactory
172 for both treatment groups with no progression of chondral wear. The PU group had >50% infill of
173 regenerative tissue in 80% of the cases that underwent second look arthroscopy at 1 year.

Kon et al [44] reported improvement in outcomes using the IKDC and Tegner score 2 years after surgery. They also showed different trends in clinical outcome, with patients undergoing combined surgery (e.g.) cartilage treatment and osteotomy, having slower improvement but achieving similar results at 2 years.

All reported clinical studies included medial and lateral meniscus groups. However in a prospective multicentre study from 6 European centres Bouyarmane et al [45] specifically looked at the more biomechanically challenging lateral side in 54 patients. Pain (VAS) and functional outcome scores (IKDC and KOOS) were improved at 2 years showing safe and effective use on the lateral side. (Table 2).

AUTHORS PREFERRED SURGICAL TECHNIQUE

Prior to implantation of the meniscal scaffold it is important to establish some key factors:

- An intact meniscal rim with sufficient tissue present both in the anterior and the posterior horns to allow for secure fixation
- A well aligned and stable knee
- A body mass index (BMI) below 35 kg/m2
- No systemic disease or infection present
- Cartilage damage should not exceed the International Cartilage Repair Society (ICRS) classification of Grade 3

Once these factors have been established the scaffold can be placed in the patient's knee at the time of partial meniscectomy using a standard arthroscopic surgery procedure and standard equipment. If it is found at the time of surgery that the medial compartment is tight, it is advised to distend the medial

collateral ligament via an outside in or inside out pie crusting technique. The surgical steps are then as follows:

(1) Debridement of the meniscal tissue should extend in the red on red or red on white zone (Figure 1)

(2) The meniscal rim is punctured to open up vascular channels and rasped to try to promote healing

(3) The defect is measured along the inner edge by a specifically designed meniscal ruler (Figure 2)

(4) The implant is then measured and cut with a scalpel (Figure 3)

- for defects <3cm long the implant is cut 3mm bigger; for defects ≥3cm long the implant is cut 5mm bigger allowing for natural shrinking as the implant is sutured

- to allow a good fit the anterior portion is cut at a 30-45◦ angle

(5) The implantation requires anteromedial and anterolateral portals, with an optional central transpatellar tendon portal (enlargement of the portal used for insertion of the device may be required). A posteromedial or posterolateral incision may also be required if an inside-out meniscal fixation technique is used

(6) Caudal and cranial surfaces are marked to avoid positioning problems then a blunt nose grabber is placed on the posterior part of the implant and this is introduced first. A vertical holding suture may be placed in the native meniscus tissue to bring implant through the eye of this holding suture (Figure 4)

(7) Fixation with horizontal all-inside suture from the posterior edge of the implant to the native meniscus. The distances between the sutures should be kept to approximately 0.5 cm. Each suture should be placed at one third to one-half of the implant's height, as determined from the lower surface of the implant (All-inside suturing has proven effective and this technique is commonly used for the posterior part of the rim. For the middle and anterior part of the rim, all-inside, inside-out or outside-in techniques can be used) (Figure 5)

(8) Using a basket punch the implant can be further trimmed or altered after fixation

If considering a lateral meniscal implantation then a similar technique is used, however there must be an intact lateral meniscal wall across the popliteal hiatus to allow for secure fixation.

POSTOPERATIVE REHABILIATAION

The patient should remain non-weight bearing for 3 weeks then start partial weighting progressing to full weight bearing over the next 5 weeks. During the first 13 weeks an unloader brace is worn. The knee is mobilised immediately on day 1 0-30° for the first 2 weeks. Then motion is increased 0-60° on week 3, then 0-90° from week 4-6, after this flexion is further increased until a full range of motion is achieved. Light exercise without pivoting (e.g.) jogging on level ground can be commenced after 13 weeks. Non contact sport may be started at 6 months at the surgeon's discretion, with 9 months recommended for more strenuous sports.

CONCLUSION

Preservation of the meniscus is important towards limiting symptoms and reducing the risk of osteoarthritic change.[8, 9]. However, in symptomatic patients following partial meniscectomy, meniscal scaffolds appear to have a useful clinical role. CMI has proven to be a safe implant with long term outcome data and promising results with improvements in functional outcome and pain scores, while preventing osteoarthritic change. This appears to occur even in the presence of some implant shrinkage and also when MRI signal is not comparable to normal meniscus tissue. The Actifit data also suggests safety and improved function/pain in patients where it has been indicated. Further longer term outcome studies are awaited to establish if this benefit is sustained. Meniscal scaffolds appear to perform best in chronic post meniscectomy patients rather than acute patients, and further randomised controlled trials including both implants would be of benefit to further define when these scaffolds would be most beneficial.

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FIGURE LEGEND

Figure 1: Debridement of meniscus to stable rim.

Figure 2: Measurement of meniscal defect.

Figure 3: Measurement and cutting of implant in relation to size of defect.

Figure 4: Marking of appropriate surfaces and anterior/posterior position of implant.

Figure 5: The meniscal implant in situ