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Meniscal implants

Indications and outcomes

The concept of meniscal implants was introduced in the early nineties in order to prevent or delay the deleterious effects of meniscal deficiency. The rationale behind the use of a meniscal scaffold was replacement of meniscal loss with a three-dimensional structure capable of supporting production of a meniscus-like fibrocartilaginous tissue. The two scaffolds currently approved and available for clinical use are described in the following sections.

The *Menaflex Collagen Meniscus Implant* (CMI®; Ivy Sports Medicine GmbH., Gräfelfing, Germany) is a porous collagen-glycosaminoglycan (GAG) matrix of defined geometry, density, thermal stability and mechanical strength [10]. It is composed of about 97% purified type I collagen, the most commonly found protein in the human body. The remaining portion of the CMI® consists of GAGs, including chondroitin sulphate and hyaluronic acid.

The type I collagen is isolated and purified from bovine Achilles tendon, then the collagen-GAG complex is chemically cross-linked to improve in vivo stability and ease handling and implantation. After in vitro studies had shown good cellular ingrowth of this three-dimensional (3D) matrix, the Menaflex CMI® was tested in animal models. These experiments initially showed no evidence of cartilage wear or damage and then showed signs of meniscal tissue regeneration [18, 19]. Subsequent animal studies confirmed these findings, showing ingrowth of the implant-regener-

ated tissue to the host meniscus rim, and increasing amounts of CMI® resorption and replacement by self-tissue over serial time points. Experiments in a canine model suggested complete CMI® resorption and replacement by 6 months. Furthermore, MRI demonstrated excellent correlation between the gross and histological observations, supporting the findings of continued tissue ingrowth and maturation over time.

The *Actifit® implant* (Orteq Ltd., London, UK) is a synthetic polymeric scaffold composed to 80% of a biodegradable polyester (polycaprolactone) and to 20% of polyurethane. The soft polyester segment provides flexibility and a constant degradation rate; while the stiff semi-biodegradable polyurethane segment provides mechanical strength. To obtain a

material with excellent mechanical properties, the polyurethane is made without a catalyst, which contributes to polymer biocompatibility and uniformity [4].

The Actifit® scaffold also underwent extensive animal testing. Canine studies revealed fully integrated scaffolds after implantation in meniscectomised joints, with evidence of meniscus-like tissue ingrowth and only minimal immunological response [21]. Further studies confirmed the safety of the scaffold, showing no deleterious effects on the articular cartilage and a friction coefficient similar to that of the native meniscus after 3 months [12, 23].

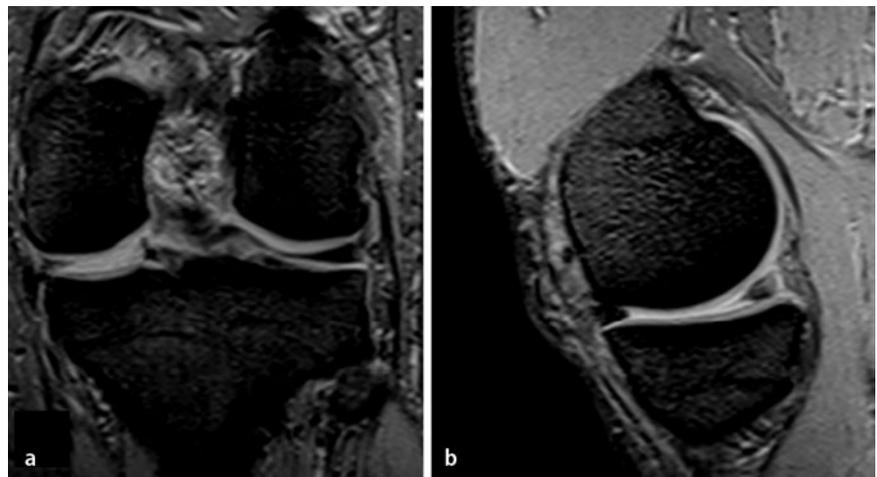


Fig. 1 ▲ MRI appearance of a medial Collagen Meniscus Implant (CMI®) 10 years after the implant on coronal (a) and sagittal (b) view. The scaffold is still clearly visible but with a reduced size and a slightly higher signal compared to native meniscus

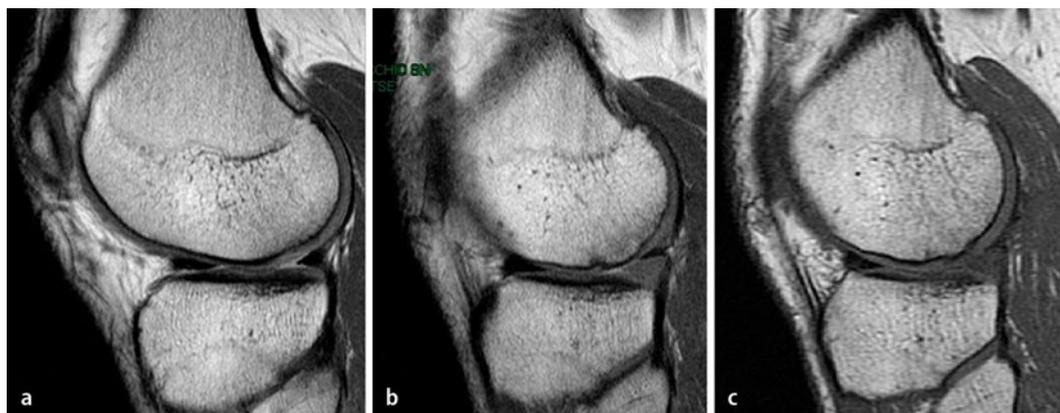


Fig. 2 ◀ Sagittal MRI slice before medial Actifit® implant (a), after 6 months (b) and after 12 months (c). Posterior horn defect filling and progressive enhancement of scaffold signal is present



Fig. 3 ▲ Arthroscopic appearance of medial Actifit® 7 months after the implant. The scaffold appears in place, with good integration with the native meniscus

Indications

Surgery for the symptomatic meniscus-deficient knee should only be considered after all nonsurgical measures (e.g. physical therapy) have proven unsuccessful. Accurate patient selection—including provision of the patient with detailed information on the long rehabilitation phase and both clinical and radiological evaluation—is mandatory in order to obtain a good outcome and prevent early failure.

The main indications for partial replacement of the meniscus with scaffolds are:

- prior loss of meniscal tissue >25%,
- irreparable meniscus tears requiring partial meniscectomy,
- traumatic or chronic posttraumatic meniscus tear,
- meniscus damage requiring greater than 25% removal
- intact anterior and posterior attachments (necessary for anchorage),

- an intact rim over the entire circumference (except for the area of the popliteal hiatus for the lateral meniscus).

In the case of anterior cruciate ligament (ACL) deficiency, this should be corrected within 12 weeks of scaffold implant. Patients must agree to a strict postoperative rehabilitation program.

The treatment of acute meniscal lesions with meniscal scaffolds is still a very controversially debated topic. A multicentre study by Rodkey et al. [15] using medial Menaflex CMI® reported no clinically relevant differences to partial meniscectomy in acute meniscal lesion at mid-term follow-up. However, there are currently no analogous studies available for Actifit®.

The main contraindications to meniscal replacement with scaffolds are:

- concomitant posterior cruciate ligament (PCL) insufficiency of the involved knee,
- untreated grade IV degenerative cartilage disease in the affected joint,
- concomitant untreated posterior knee instability,
- uncorrected axis deviation,
- systemic or local infection,
- evidence of osteonecrosis in the involved knee.

Generally, advanced chondral degeneration represents the most common contraindication; however if this can be addressed beforehand or simultaneously—with autologous chondrocyte transplantation, osteochondral grafting or synthetic scaffolds in case of localised chondral de-

fects—meniscus implants can indeed be considered.

» Advanced chondral degeneration represents the most common contraindication

Malalignment is also reported to cause abnormal pressure on the affected compartment; therefore, prior or simultaneous corrective osteotomy should be considered in the case of noticeable axis deviation. Furthermore, rheumatic diseases like rheumatoid arthritis, relapsing polychondritis, severe degenerative osteoarthritis and inflammatory arthritis should discourage scaffold implant.

Prophylactic meniscus scaffold implant in the absence of symptoms remains a controversial issue and cannot currently be routinely recommended. This remains an option for individual cases only (e.g. subtotal loss of a lateral meniscus in adolescents with valgus knee).

With both meniscus implants, surgery is generally performed arthroscopically, with the scaffold inserted into the joint through enlarged arthroscopic portals. Following size determination and preparation of the residual meniscus, the meniscus implant is fixed to the meniscal remnant and capsule using new-generation all-inside, or a combination of all-inside and inside-out suture devices.

Outcomes

Due to its early availability in the nineties, the Menaflex CMI® has been extensively studied. Clinical results have been

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Meniscal implants. Indications and outcomes

Abstract

Introduction. Meniscal scaffolds represent an attractive surgical option for patients with persisting symptoms following partial meniscectomy.

Methods. Two different scaffolds are currently approved and available for clinical use in Europe: the Collagen Meniscus Implant (CMI®; Ivy Sports Medicine GmbH., Gräfelting, Germany), a porous collagen-glycosaminoglycan (GAG) matrix of defined geometry, composed of about 97% purified type I collagen; and the Actifit® Implant (Orteq Ltd., London, UK), a synthetic polymeric scaffold composed of 80% biodegradable polyester and 20% polyurethane.

Results. With strict observation of the correct differential indications, good/excellent improvement of knee function and increased sports activities can be expected in 70–90% of patients. Additional pathologies, such as chondral degeneration, instabilities and malalignments must be considered.

Conclusion. Although a wide range of conditions could potentially be treated, good results are strictly dependent on close observation of the correct indications.

Keywords

Knee · Partial meniscal resection ·
Rehabilitation · CMI® · Actifit®

presented in several studies which also reached long-term follow-ups. Satisfying outcomes have been reported in about 70% of patients [7], with knee function and pain reduction maintained from the short to the long term [6]. The cornerstone study of Menaflex CMI® surgery is represented by the multicentre randomized controlled trial performed by Rodkey et al. [15]. This study involved about 300 patients and compared medial Menaflex CMI® implantation to medial meniscectomy after 5 years of follow-up. Whereas better results and lower reoperation rates were reported in patients with chronic meniscal deficiency treated with the CMI® implant, for patients with acute meniscal lesions, no significant differences were found between the two groups. This thus limits the strict, evidence-based indication of Menaflex CMI® to patients with previous meniscectomy.

The potential long-term chondroprotective effect of the scaffold was studied by Zaffagnini et al. [27] in a controlled clinical trial. This study revealed fewer radiological signs of knee osteoarthritis and better clinical results in patients treated with medial Menaflex CMI®, particularly in terms of pain and knee function. Good results have also been reported for lateral Menaflex CMI® [8, 26, 28]. Overall, the clinical results appeared to improve after 6 months, to reach their peak at the 1-year follow-up and to remain almost stable for 10 years of follow-up.

Regarding combined procedures, Bulgheroni et al. [2] reported the long-term results of combined ACL reconstruction and medial Menaflex CMI® compared to ACL reconstruction and partial medial meniscectomy. The authors showed less postoperative pain in patients with chronic meniscal lesions and reduced laxity in patients with acute meniscal tears when treated with medial Menaflex CMI®. Hirschmann et al. [8] reported a case series of 67 patients, of whom 53 were treated with medial or lateral CMI combined with ACL reconstruction. These authors showed a wider area of bone marrow oedema and worse clinical results compared to isolated Menaflex CMI® at the 1-year follow-up.

Linke et al. [11] performed a controlled study involving 60 patients with varus

morphotype and medial meniscus loss. In this study, no significant difference could be shown in the short term between patients who underwent high tibial valgus osteotomy (HTVO) plus medial Menaflex CMI® and those who only underwent HTVO. Other authors reported good results after combined Menaflex CMI® implantation and microfractures or matrix-associated autologous chondrocyte implantation (MACI) [16, 20, 24].

Histological specimens obtained during second-look arthroscopies revealed the presence of regenerated tissue similar to the native fibrous meniscal cartilage after 6 months [20], inhibition of osteoarthritic degeneration at 24 months follow-up [14] and progressive resorption of the scaffold with complete absence of the implant at 5 years [3]. A recent systematic review evaluating the appearance of CMI with MRI showed a progressive reduction of scaffold size during early follow-ups, accompanied by a slower reduction of signal intensity approaching an iso-intense signal pattern analogous to that of normal meniscus (■ Fig. 1; [5, 25]).

The clinical experience with Actifit® is still limited, due to its late European Union regulatory approval for sale in July 2008. However, the available results are promising and do not appear to be inferior to those obtained with Menaflex CMI®. The main clinical data derive from a single multicentre European study involving 52 patients with irreparable medial and lateral lesions or meniscal defects caused by previous meniscectomy. Clinical evaluation showed a significant improvement of knee function, pain and sports activities after 6 months, with maintenance of the results at 12 and 24 months.

The 2-year reoperation and failure rate in the abovementioned study was 17.3%—mostly due to the implant procedure and not to the scaffold itself. Only 7% of the adverse events registered during the follow-up were related to the scaffold; these were mostly knee pain, effusion and swelling. The lateral meniscus appeared to present a higher rate of failures.

■ **The 24-month MRI follow-up evaluation revealed cartilage status to be stable or slightly improved in 92% of cases.**

In 82% of patients, the MRI evaluation also showed significant enhancement of the scaffold signal with time, a sign of tissue ingrowth and vessel proliferation (■ Fig. 2, [22]). Furthermore, the second-look arthroscopy showed good integration of the scaffold with the native meniscus, with no suture loosening (■ Fig. 3). Histological examination at 12 months revealed fully vital material, no adverse reaction to the scaffold material and a regenerated tissue composed of type I collagen, fibroblasts and fusiform fibrochondroblast-like cells [23].

Other case series [1, 9] have reported similar results: Kon et al. [9] showed good knee function improvement and return to sports activities in a single-centre cohort of 18 patients; while Bouyarmene et al. [1] demonstrated similar results in a group

of patients treated exclusively with lateral Actifit® scaffolds.

The short-term results with both Menaflex CMI® and Actifit® have been reported in a small prospective study which showed no substantial differences [17]. Moreover, both scaffolds have been successfully used by Marcacci et al. [13] to treat unicompartamental osteoarthritis through an integrated biomechanical and biological approach alternative to metal resurfacing, involving combined ACL reconstruction, knee osteotomy and cartilage reconstruction with an osteochondral biomimetic scaffold, depending on the main specific joint requirements.

Risks and complications

Only a few risks directly related to the device have been reported for Menaflex CMI® and Actifit®. However, most of the complications are mainly caused by a less than perfect surgical technique. Saphenous nerve injury has been reported after medial scaffold implant, as a possible consequence of suture placement [3].

Knee instability could theoretically represent a drawback of the excessive medial or lateral release performed to allow opening of the corresponding compartment [15]; while popliteus tendon entrapment could be caused by improper scaffold fixation when the popliteal hiatus is involved.

Other complications like pain, swelling, wound infection and deep vein thrombosis have also been reported in the different studies present in the literature, with frequencies ranging from 0 to 32%, depending on the follow-up. The total failure and reoperation rate for meniscal implants is about 10% at mid-term, the main causes being persistent pain, swelling, infection or mechanical failure of the scaffold.

Conclusion

- Meniscal scaffolds represent an attractive surgical option for patients with persistent pain following partial meniscal resection,
- With strict observation of the correct indications, good/excellent improvement of knee function and increased

sports activities can be expected in 70–90% of patients.

- Additional pathologies, such as chondral degeneration, instabilities and malalignments must be considered.
- Although the range of conditions treated by the implants could potentially be wider, the paucity of data currently prevents a recommendation for their routine use as an alternative to partial meniscal resection,
- In terms of a potential chondroprotective effect, there is a particular lack of long-term data for the Actifit® scaffold.

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Compliance with ethical guidelines

Conflict of interest. S. Zaffagnini, C. Fink, A. Grassi, G. M. Marcheggiani Muccioli and M. Marcacci state that there are no conflicts of interest.

The accompanying manuscript does not include studies on humans or animals.

References

1. Bouyarmine H, Beaufile P, Pujol N et al (2013) Polyurethane scaffold in lateral meniscus segmental defects: clinical outcomes at 24 months follow-up. *Orthop Traumatol Surg Res*. doi:10.1016/j.otsr.2013.10.011
2. Bulgheroni E, Grassi A, Bulgheroni P et al (2014) Long-term outcomes of medial CMI implant versus partial medial meniscectomy in patients with concomitant ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc*
3. Bulgheroni P, Murena L, Ratti C et al (2010) Follow-up of collagen meniscus implant patients: clinical, radiological, and magnetic resonance imaging results at 5 years. *Knee* 17(3):224–229
4. Groot JH de, Vrijer R de, Pennings AJ et al (1996) Use of porous polyurethanes for meniscal reconstruction and meniscal prostheses. *Biomaterials* 17(2):163–173
5. Genovese E, Angeretti MG, Ronga M et al (2007) Follow-up of collagen meniscus implants by MRI. *Radiol Med* 112(7):1036–1048

6. Grassi A, Zaffagnini S, Marcheggiani Muccioli GM et al (2014) Clinical outcomes and complications of a collagen meniscus implant: a systematic review. *Int Orthop*
7. Harston A, Nyland J, Brand E et al (2011) Collagen meniscus implantation: a systematic review including rehabilitation and return to sports activity. *Knee Surg Sports Traumatol Arthrosc* 20(1):135–146
8. Hirschmann MT, Keller L, Hirschmann A et al (2013) One-year clinical and MR imaging outcome after partial meniscal replacement in stabilized knees using a collagen meniscus implant. *Knee Surg Sports Traumatol Arthrosc* 21(3):740–747
9. Kon E, Filardo G, Zaffagnini S et al (2012) Biodegradable polyurethane meniscal scaffold for isolated partial lesions or as combined procedure for knees with multiple comorbidities: clinical results at 2 years. *Knee Surg Sports Traumatol Arthrosc*
10. Li S-T, Rodkey WG, Yuen D et al (2002) Type I collagen-based template for meniscus regeneration. In: Lewandrowski K-U, Wise DL, Trantolo DJ, Gresser JD, Yaszemski MJ, Altobelli DE (Hrsg) *Tissue engineering and biodegradable equivalents*. Scientific and clinical applications. Marcel Dekker, New York, pp 237–266
11. Linke RD, Ulmer M, Imhoff AB (2006) Replacement of the meniscus with a collagen implant (CMI). *Oper Orthop Traumatol* 18(5–6):453–462
12. Maher SA, Rodeo SA, Doty SB et al (2010) Evaluation of a porous polyurethane scaffold in a partial meniscal defect ovine model. *Arthroscopy* 26(11):1510–1519
13. Marcacci M, Zaffagnini S, Kon E et al (2013) Unicompartamental osteoarthritis: an integrated biomechanical and biological approach as alternative to metal resurfacing. *Knee Surg Sports Traumatol Arthrosc* 21(11):2509–2517
14. Rodkey WG, Steadman JR, Li ST (1999) A clinical study of collagen meniscus implants to restore the injured meniscus. *Clin Orthop Relat Res* 367(Suppl):S281–S292
15. Rodkey WG, DeHaven KE, Montgomery WH III et al (2008) Comparison of the collagen meniscus implant with partial meniscectomy. A prospective randomized trial. *J Bone Joint Surg Am* 90(7):1413–1426
16. Ronga M, Grassi FA, Manelli A, Bulgheroni P (2006) Tissue engineering techniques for the treatment of a complex knee injury. *Arthroscopy* 22(5):576.e1–3
17. Spencer SJ, Saithna A, Carmont MR et al (2012) Meniscal scaffolds: early experience and review of the literature. *Knee* 19(6):760–765
18. Stone KR, Rodkey WG, Webber RJ et al (1990) Future directions. Collagen-based prostheses for meniscal regeneration. *Clin Orthop Relat Res* 252:129–135
19. Stone KR, Rodkey WG, Webber R et al (1992) Meniscal regeneration with polymeric collagen scaffolds. In vitro and in vivo studies evaluated clinically, histologically, and biochemically. *Am J Sports Med* 20(2):104–111
20. Stone KR, Steadman JR, Rodkey WG, Li ST (1997) Regeneration of meniscal cartilage with use of a collagen scaffold. Analysis of preliminary data. *J Bone Joint Surg Am* 79(12):1770–1777
21. Tienen TG, Heijkants RG, Groot JH de et al (2006) Replacement of the knee meniscus by a porous polymer implant: a study in dogs. *Am J Sports Med* 34(1):64–71

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22. Verdonk P, Beaufils P, Bellemans J et al (2012) Successful treatment of painful irreparable partial meniscal defects with a polyurethane scaffold: two-year safety and clinical outcomes. *Am J Sports Med* 40(4):844–853
 23. Verdonk R, Verdonk P, Huisse W et al (2011) Tissue ingrowth after implantation of a novel, biodegradable polyurethane scaffold for treatment of partial meniscal lesions. *Am J Sports Med* 39(4):774–782
 24. Zaffagnini S, Giordano G, Vascellari A et al (2007) Arthroscopic collagen meniscus implant results at 6 to 8 years follow up. *Knee Surg Sports Traumatol Arthrosc* 15(2):175–183
 25. Zaffagnini S, Grassi A, Marcheggiani Muccioli GM et al (2014) MRI evaluation of a collagen meniscus implant: a systematic review. *Knee Surg Sports Traumatol Arthrosc*
 26. Zaffagnini S, Marcheggiani Muccioli GM, Bulgheroni P et al (2012) Arthroscopic collagen meniscus implantation for partial lateral meniscal defects: a 2-year minimum follow-up study. *Am J Sports Med* 40(10):2281–2288
 27. Zaffagnini S, Marcheggiani Muccioli GM, Lopomo N et al (2011) Prospective long-term outcomes of the medial collagen meniscus implant versus partial medial meniscectomy: a minimum 10-year follow-up study. *Am J Sports Med* 39(5):977–985
 28. Zaffagnini S, Marcheggiani Muccioli GM, Grassi A et al (2011) Arthroscopic lateral collagen meniscus implant in a professional soccer player. *Knee Surg Sports Traumatol Arthrosc* 19(10):1740–1743