Degenerative joint disease following meniscectomy has been a well-known phenomenon since King and Fairbank focused attention on the process over 50 years ago. In recent years the extreme importance of the meniscus cartilage in the complex biomechanics of the knee joint has been well documented. The meniscus has functions in load bearing, load transmission, joint stability, lubrication and proprioception and is extremely important in reducing the incidence of degenerative joint disease. Arthroscopic partial meniscectomy and meniscus repair have improved clinical results following meniscus lesions. However, this is not possible in every case, and a substantial number of patients still suffer the ill effects of loss of the meniscus cartilage. Replacement of a portion of or the entire meniscus seems to be an appropriate approach to prevent osteoarthritis of the knee after meniscectomy that removes a substantial portion of the meniscus. Meniscus allograft procedures have been widely used in recent years and the limited results are promising, especially in terms of pain relief. However, the technique is demanding and the correct indications are strictly limited. Because the procedure is a complete meniscus substitution, its use is not feasible for partial meniscectomy. Moreover, there is a risk of disease transmission, albeit low, and long-term follow-up shows that the results tend to deteriorate with time.

Tissue engineering holds great promise in the regeneration of damaged tissues, especially the meniscus, as described by Arnoczky. Stone and colleagues developed a bioresorbable collagen matrix in an effort to regenerate the lost meniscus tissue. The collagen meniscus implant (CMI; ReGen Biologics, Inc., Franklin Lakes, New Jersey) is fabricated from bovine Achilles tendons, obtaining a scaffold of purified type I collagen fibres, which is swollen in hyaluronic acid and chondroitin sulphate, homogenised and supplemented with glycosaminoglycans. The promising principle of this bioengineered device is the exploitation of the spontaneous structural regeneration of new autogenous meniscus tissue after meniscectomy, as first suggested by Mandl in 1929. Stone and colleagues first described the formulation and fabrication of this material. The collagen scaffold developed allows and supports the ingrowth and regeneration of new meniscus tissue, as demonstrated after the first in vitro and in vivo laboratory trials. Since then it has been used in patients undergoing partial meniscectomy to restore the shape and function of the meniscus. Recently, Steadman published the five- to six-year results of his feasibility study, with highly satisfactory results.

With this same goal, we used this device in selected patients according to suggested indications in a clinical trial. The goals of this study were to evaluate both subjective and objective results of the collagen meniscus implant at six- to eight-year follow-up.

Material and Methods

Between September 1997 and January 1999, eight patients underwent collagen meniscus implantation. The intervention was proposed to patients who had an irreparable meniscus tear or a previous major loss of meniscus cartilage after partial meniscectomy (see Figure 1). Involved knees had to be stable or surgically stabilised at the time of the implantation procedure. Both traumatic and degenerative loss of meniscus cartilage were included in the study. As suggested by Rodkey and colleagues, we excluded patients with Outerbridge grade IV chondral lesions, inflammatory or systemic diseases, collagen allergies, autoimmune diseases or pregnancy.

All eight patients gave their written informed consent before intervention. Although the implant procedure was open to both men and women, all eight patients in our study group were men. Their average age was 31 years (range 20–51 years). The meniscus lesion was located in the right knee in five cases, while in the other three cases the left knee underwent the procedure.

Three patients received a CMI in the acute setting at the time of the medial meniscectomy for irreparable meniscal lesion. In the other five cases, a subtotal meniscectomy had previously been performed. In two cases previous meniscectomy was associated with an anterior cruciate ligament (ACL) reconstruction. A grade III chondral lesion was...
detected in one case on the medial femoral condyle, and it was treated with microfractures. In four cases a grade II chondral lesion was detected on the medial femoral condyle, while in the other three cases treated acutely no chondropathy was observed at the time of surgery. All patients prospectively underwent radiographic and magnetic resonance imaging (MRI) evaluation of the involved knee, and clinical evaluation was performed using the Cincinnati Knee Rating System (CKRS)26,27 and the International Knee Documentation Committee (IKDC) evaluation form.44

Surgical Technique and Post-operative Protocol
The surgical technique for implantation included an arthroscopic procedure to evaluate meniscus loss and any other lesion of the knee. In all cases a full-thickness defect was observed. Any damaged and irreparable tissue was removed until healthy tissue was reached. In seven cases debridement reached the red–red zone of the host meniscus, while in one case reaching the red–white zone was sufficient. In all cases, bleeding of the host tissue was obtained by perforating it with a microfracture awl. The size of the defect was then determined using a specially designed measuring device, and the collagen meniscus implant was measured and trimmed to fill the defect. In every case the damaged meniscus was medial. The location of the lesion was mostly posterior and central (see Figure 2). The average length of the implant was 34mm, with a range of 25–45mm. The prepared implant was then delivered into the joint through a dedicated specimen and inserted into the defect. The implant was sutured to the host meniscus with a standard in–out suture technique. Two to six (average four) size 2–0 non absorbable sutures were utilised to secure the implant, and its stability was tested with a probe on completion of suturing.

Physical therapy was started on the first post-operative day, and continuous passive motion was immediately allowed from 0 to 60°. The passive range of motion (ROM) was increased to 0–90° after four weeks, and after two more weeks unlimited passive motion was allowed. During the first six weeks weight-bearing was not allowed, and patients walked using crutches (most patients usually used one crutch in this period). After this period, full weight-bearing was started. All patients followed a rehabilitation protocol for six months until they returned to full unrestricted physical activity.

Follow-up
All patients were evaluated regularly in the immediate post-operative period, and clinical evaluation was performed6,10,20,23 for six to eight years, with an average follow-up time of 6.8 years. The clinical examination was performed using the subjective CKRS26,27 and the objective IKDC evaluation form.44 Pain self-evaluation was measured on a visual analogue scale graded from 0 to 10. A one-leg hop test was performed from six months after the implant, and thigh diameter was bilaterally measured at mid-patellar level 5 and 15cm above the patella. Patient self-assessment was obtained from the IKDC form.

Radiographic and MRI examinations were performed two and six years after surgery and compared with the original pre-operative images. X-rays and MRI were examined by an independent radiologist40 to check for implant signal alterations, cartilage and joint space narrowing. The radiographic examination included standard anterior–posterior (AP) and lateral (LL) views to evaluate the medial joint heights using a calliper. In three cases we were able to perform an arthroscopic second look to evaluate the regenerated tissue. However, none of the patients consented to a biopsy examination.

Because of the small number of patients included in the study, no statistical analyses were performed.

Results
All eight patients underwent a final follow-up evaluation six to eight years after placement of the collagen meniscus implant. There were no complications related to the device. The mean age at the time of follow-up was 39 years (minimum 28 years, maximum 57 years).

All patients were able to return to their previous daily life activities without any limitations a mean of three months post-surgery.
Arthroscopic Collagen Meniscus Implants – Results at Six- to Eight-year Follow-up

Functional assessment based on the CKRS improved in all eight patients from pre-operative examination to final follow-up examination. The maximum functional score was achieved in five cases (see Table 1). In two cases the final observation time score was slightly lower than the two-year follow-up score, but still better than the pre-operative score. The pre-operative IKDC score showed three B and five C grades. Objective IKDC score evaluation showed improvement in all cases. In seven cases grade A was recorded at one- and two-year follow-up (see Table 2). Six years after the implantation, loss of 10° of flexion in two patients reduced their IKDC grade to B. The other five cases remained at level A grade at final term follow-up.

Table 2: International Knee Documentation Committee Scores

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<th>Patient Number</th>
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<th>1 Year After Surgery</th>
<th>2 Years After Surgery</th>
<th>6.8 Years After Surgery</th>
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Table 3: Pain Patient Self-assessment

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Mild effusion was present in only two cases during prolonged sport activities, while the other cases can perform sports without any difficulties. Subjective evaluation of pain was graded as 5, 6 or 7 in six cases before intervention. In two cases a lower grade of pain was described. At the two-year follow-up examination, seven patients reported no pain (see Table 3). In four cases the absence of pain remained for six years after surgery, while in four patients a low level of pain was described.

Thigh girth measurements showed no or slight differences between two sides; the diameter difference was never greater than 1cm. ROM compared with the opposite leg was normal in five cases, while in two cases a 10° flexion deficit was observed. A combined flexion (15°) and extension (5°) deficit was recorded in one case only. Stability was normal in all cases; in fact, in the two cases where a previous ACL reconstruction had been performed, the KT 1000 evaluation showed a <3mm difference between the operated and non-operated leg. Finally, knee function based on patient self-assessment was defined as normal or nearly normal for all patients at all follow-up examinations, as was the one-leg hop test.

At radiographic evaluation six patients had preserved articular cartilage and joint space, and they had no changes compared with pre-operative images (see Figure 3). Two patients with pre-existing grade 2 arthritis remained unchanged, while another two patients showed a slight increase in arthritis at six years after collagen meniscus implantation with decreased height of 1mm compared with the pre-operative X-ray.

MRI evaluation showed mixoid degeneration signal at the implant site in five cases (see Figures 4 and 5), while one patient had no recognisable implant. Two patients had a normal signal, with a small implant size (see Figure 6). The cases that had increased degeneration on the medial side were noted to have a mixoid degeneration implant signal on MRI. The appearance of the generated tissue showed a tendency to continue maturation in four cases, while in three cases the MRI images remained similar at the two-year control and in one case the implant disappeared.

In three cases we were able to perform a second-look arthroscopic evaluation at two years post-implantation. This revealed the presence of new tissue in two cases, although of less volume than the original implant. In the third patient there was minimal new tissue. In two cases the chondral surface was intact with no sign of degeneration, while in one case the grade 3 pre-operative arthritis was unchanged.

Discussion

Our small series of eight patients prospectively followed for a mean 6.8 years of follow-up has shown highly satisfactory clinical results for all cases.
In 1999, Rodkey and colleagues published the promising results of a two-year follow-up clinical study that demonstrated improvement of eight patients who underwent a CMI implantation. The five-year results published recently by Steadman confirmed the capacity of the implant to maintain its function and structure without negative effect, with significant improvement compared with pre-operative status. In fact, clinically the results were maintained with 88% improvement, with only a small deterioration of results at the final follow-up. Moreover, at radiographic evaluation Steadman was able to show an MRI signal similar to mature fibrocartilage, with no sign of chondral degeneration.

Our clinical results at a mean of 6.8 years of follow-up agree with the findings reported by Rodkey and colleagues and Steadman. In our series, five patients had already undergone a previous partial meniscectomy, which could have increased the risk of clinical worsening at long-term follow-up, as in Steadman’s series. However, deterioration of the results and reduced height of the medial rim were observed in only two cases.

It is interesting to note that these two cases showed a decreased ROM from two- to six-year follow-up. These changes could be partially related to the surgery and partially to normal joint evolution related to patient age at the time of the follow-up control. In fact, these two patients were the oldest in this group (43–51 years old at the time of surgery). These findings are supported by the fact that at radiographic and MRI follow-up there were minimal progressive degenerative changes in the area of the implanted scaffolds compared with the pre-operative examinations. This observation is even more important considering that five of our eight patients were noted to have Outerbridge grade II or III chondral damage prior to placement of the CMI.

The second-look arthroscopic examinations demonstrated a partial resorption of the implant. These data are similar to the reports of Carter, Milachowsky and Wirth, who have shown a shrinkage of the implanted meniscus allograft at short- and long-term follow-up, especially when lyophilised grafts were used.

A well-matured posterior horn was observed in only two cases with good clinical results, while other cases showed an incomplete restoration of tissue quality. These findings are similar to reports by Verstrate and Van Arkel looking at MRI and clinical outcome in cases of meniscus transplantation. These data are different from those reported in the recent study by Steadman, who revealed a well-matured meniscal structure. This difference could be related to different activity levels being reached after surgery or varying quality of the MRI examination performed.

Another important factor that can influence the histological response and quality of MRI findings is the biomechanical and architectural features of the device. Milachowski and co-workers have shown that deep-frozen and lyophilised allograft meniscus do not reach the tensile strength of normal meniscus; the CMI has lower initial mechanical characteristics and a different internal design compared with the normal meniscus. We were not able to determine the mechanical properties of the newly formed tissue; however, at second-look and MRI control the quality of the tissue seemed inferior to the original meniscal tissue.

The most prominent limitation of this study was the sample size of only eight patients. However, this was the first experience in Europe of such a material and all cases were followed longitudinally through all of the clinical and radiographic aspects.
Conclusion

In conclusion, the results of a pioneering tissue engineering technique for meniscal regeneration are encouraging. The scaffold used in this group of patients is the one that Li et al. and Rodkey et al.20,21,46 developed in the early 1990s. This collagen meniscus scaffold has shown interesting results in both animal studies20,41–43 and clinical experience,20,21,23,24,41–43,46 even at six-year follow-up. The ability to trim the collagen implant to fit an existing or created meniscus defect without compromising the entire meniscus structure makes the CMI unique device that tries to restore the important roles of the meniscus while eliminating problems related to the sizing and disease transmission typical of meniscal allograft transplantation.21,41,42,43 Our X-ray results, as well as those of Steadman, show that this device could be used to delay the natural evolution of a partially meniscectomized joint into early degenerative status, although the limitation in terms of progression of degenerative joint disease compared with isolated partial meniscectomy has not yet been completely resolved. The implant allows patients to return to physical activity without any adverse effect to the joint and with similar X-ray findings to the pre-operative condition. A natural evolution of this technique, which we have now used for the last two years, is an all-inside technique for suture application. These devices are particularly useful to avoid the posterior medial incision and related complications. We have been able to decrease the operative time, and the all-inside devices are much easier to apply in tight knees. Further improvement to restore normal meniscus function and to avoid degenerative joint disease might include the improvement of the mechanical and structural characteristics of the collagen meniscus implant so that the device is more similar to normal meniscus cartilage. Finally, the application of stem cells or growth factors to the implanted device could increase the biological response and remodelling process of this structure.

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Arthroscopic Collagen Meniscus Implants – Results at Six- to Eight-Year Follow-up

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