The effects of meniscal allograft transplantation on articular cartilage
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Chapter 8

Meniscal Allograft Transplantation.
Part II: Alternative Treatments, Effects on Articular Cartilage, and Future Directions

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Abstract

Meniscal allograft transplantation in clinical practice has progressed to a point where relief of pain may be expected for the short term. However, it remains to be established whether a transplanted meniscus can prevent degenerative changes in the knee joint on the long term. In part 2 of this review, meniscus regeneration and alternative treatments to meniscal allograft transplantation will be evaluated as well as the effect of meniscal allograft transplantation on articular cartilage. Remaining questions and future directions will be considered in a final discussion. It can be concluded that considerably more data and evaluations of results are needed to determine whether meniscal allograft transplantation in humans will be successful in protecting and preserving articular cartilage after meniscectomy on the long term.
Introduction

Meniscal allograft transplantation has been studied by many as an alternative to meniscectomy. Part 1 of this review (chapter 2) discussed the background and results of meniscal allograft transplantation and the selection and preservation of allografts followed by surgical considerations. In part 2 meniscus regeneration and alternative treatments to meniscal allograft transplantation are evaluated as well as the effects of meniscal transplantation on articular cartilage. Remaining questions and future directions are taken into consideration in a final discussion. The aim of this review is to evaluate the potentials of meniscal allograft transplantation to prevent degenerative changes of the articular cartilage.

Meniscus Regeneration and Alternative Treatments

Meniscus Regeneration

Various experimental and clinical studies have described meniscal regeneration following meniscectomy. Smillie erroneously concluded that meniscus regeneration was only possible after total meniscectomy and not after partial meniscectomy. In a dog study, Arnoczky et al. found a remodeling response in 67% of the menisci after partial meniscectomy as well. Histological studies of regenerated menisci suggest that fibroblasts migrate from the synovium into the joint, become undifferentiated, and, subsequently, differentiate into chondrocytes. However, Ghosh et al. noted that the tissue that regenerates is not true fibrocartilage, but consists of loosely dispersed collagen fibers and that the proteoglycan content is lower than normal. It has been demonstrated in rabbits and dogs that degenerative changes of articular cartilage in the tibiofemoral joints are inversely related with the size of the regenerated meniscus. In a rabbit study, Moon et al. showed a higher incidence of meniscal regeneration after medial than after lateral meniscectomy. This may be a cause of poorer results after lateral meniscectomy as compared with medial meniscectomy.

In general, it is assumed that incompletely regenerated menisci fail to prevent degenerative joint disease.

Meniscal Autografts

Stone et al. reimplanted fresh meniscal autografts in dogs immediately after meniscectomy and noted that 7 of 14 autografts failed to heal at 1 to 12 months follow-up, whereas meniscal cartilage showed significant abnormalities in collagen organization both at the healing interface and within the substance of the replant. These abnormalities may compromise long-term structural properties of meniscal tissue and limit its functional behavior. It was concluded that these grafts are inadequate substitutes for intact menisci. In contrast, Szomor et al. reimplanted 8 fresh medial meniscal autografts in sheep knees and showed uneventful healing to
the capsule. All grafts showed a normal or nearly normal histological appearance at 4 months follow-up and noticeable but not complete protection against damage to articular cartilage.

Autografts consisting of the middle third of the patellar tendon in sheep demonstrated the same revascularization process and cellular repopulation as meniscal allografts at 1 year follow-up.\(^{29}\) Although these tendon autografts offered some cartilage protection, the biomechanical properties were inferior to genuine meniscal tissue. Bruns et al.\(^ {30}\) performed meniscus replacement in 12 sheep using strips of autologous perichondrium harvested from the lower rib with 3 to 12 months follow-up. In all transplanted knee joints, a new perichondral meniscus developed after 3 months with a normal orientation of collagen fibers and normal cellular characteristics, but in the central region areas of calcification were observed. Moreover, vascularization of perichondral menisci was reduced when compared with normal menisci and failure stress and tensile modulus were significantly lower. Femoral and tibial cartilage in contact with the autografts showed slight surface irregularities in 1 animal. In a rabbit study, periosteal autografts were implanted in partial meniscal defects, which differentiated into bone and hyaline cartilage that was ineffective as meniscus and the knees showed accelerated articular degeneration.\(^ {31}\) Transplantation of a pediculated infrapatellar fat pad in sheep showed promising macroscopical results with the development of a meniscus-like structure within 6 months.\(^ {32}\) However, this structure deteriorated at 1 year follow-up. Mechanically, it remained very weak and was never comparable to meniscal tissue. In a pilot study, Johnson and Feagin\(^ {33}\) implanted 4 semitendinosus tendon grafts and 1 patellar tendon graft in the lateral compartment of meniscectomized human knee joints. Only 1 patient showed minimal clinical improvement; the others did not show any improvement. At second-look arthroscopy in 4 patients at 9 to 24 months after implantation, preservation of articular cartilage was not observed. It was concluded that these autogenous grafts were not successful as a substitute for an absent meniscus. In another clinical study, Kohn\(^ {34}\) replaced the medial meniscus by a quadriceps tendon graft in combination with anterior cruciate ligament reconstruction followed by clinical, radiological, and/or arthroscopical evaluation at 1 to 2 years after reconstruction. Progress in osteoarthrosis was not observed radiologically, but in 2 of 9 patients progress of chondromalacia was observed arthroscopically. In addition, range of motion was decreased but stability in 70° flexion was improved after meniscus replacement in combination with anterior cruciate ligament reconstruction as compared with a control group that underwent anterior cruciate ligament reconstruction only. In conclusion, there is no proof at present that replacement of menisci by autografts can protect the articular cartilage from degeneration on the long term.

**Meniscal Prostheses**

At present, there are no artificial materials available with properties similar to a normal meniscus.\(^ {34}\) Sommerlath and Gillquist\(^ {35}\) implanted meniscal prostheses made
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of Dacron (Dupont, Wilmington, DE, USA) with polyurethane coating in meniscectomized rabbit knees and found at 3 months follow-up that the prosthesis group showed less changes in the articular cartilage of the tibia, but not of the femur, as compared with the meniscectomy group. Biomechanically, the structural properties of the knee containing a prosthesis were more similar to that of meniscectomized knees than to that of a normal knee. In a dog study, Klompmaker et al. investigated the properties of a porous polyurethane meniscus prosthesis and demonstrated initial ingrowth of fibrous tissue containing type I collagen only. From 10 weeks onwards, the prostheses were invaded with fibrocartilage strongly resembling normal meniscal fibrocartilage containing both type I and II collagen. It was concluded that porous polymers can be useful for replacement of the meniscus although cartilage degeneration was frequently observed. A prosthesis made of a polytetrafluoroethylene net of nondegradable fibers was reported to provide cartilage protection in dogs up to 1 year after implantation. After an initial response consisting of infiltration with inflammatory cells and fibroblasts, fibrocartilage developed at 9 months follow-up. In another study, a polyester carbon fiber prosthesis implanted in rabbits did not show any ingrowth of tissue, whereas biological regeneration was poor and a severe inflammatory response occurred. However, some protective effects on the cartilage were found as well.

In summary, it can be stated that most synthetic polymeric materials fail at present to approximate the properties of normal menisci and, therefore, cannot protect articular cartilage on the long term. More research is needed to optimize biomaterials for meniscal prostheses.

Resorbable Scaffolds

Resorbable scaffolds can be used successfully as nerve conduits and as replacement of human skin. Because chondrocytes most likely do not survive meniscal transplantation, it has been suggested that meniscal autografts or allografts are in practice mere biological scaffolds for meniscal regeneration. Stone et al. investigated meniscal reconstruction by meniscal regeneration supported by scaffolds that are designed to support ingrowth of host fibroblasts and/or chondroblasts in a sequence of animal trials. In dog knees that underwent excision of 80% of the meniscus, host chondrocytes were observed to be present in an implanted scaffold of collagen purified from bovine Achilles tendon with only a minimal immunological response at 1 year follow-up.

In a clinical trial, newly formed collagen was found in biopsies taken at second-look arthroscopy performed at either 3 or 6 months after implantation. Furthermore, magnetic resonance imaging (MRI) showed signal maturation in the regenerated meniscus during a 3-year follow-up. Nevertheless, it is to early to conclude whether meniscal scaffolds made of collagen or biodegradable materials can sufficiently protect articular cartilage in humans on the long term.
Xenografts
Xenografts are theoretically still the easiest obtainable material to replace menisci. In experimental studies in dogs and rabbits, porcine small intestinal submucosa has been used to replace meniscal tissue.\textsuperscript{46,47} At 12 and 24 weeks follow-up, respectively, replacement tissue closely resembled normal meniscal tissue with respect to chondrocyte differentiation and collagen content. In clinical practice, implantation of meniscal xenografts has not yet been reported because shape and biochemical characteristics of menisci from animals are different from those of humans. Furthermore, in comparison to allografts, xenografts can induce strong immunological rejection processes that are currently incompletely defined.\textsuperscript{48}

Articular Cartilage
Although meniscal allograft transplantation appears to be attractive, only a few experimental studies have been published with respect to the ability of a meniscal allograft to protect the articular cartilage. Changes in articular cartilage as observed after meniscal transplantation in humans are summarized in Table 2 in Part 1 of this review (Chapter 2).

Macroscopical Findings
Shibuya\textsuperscript{49} observed osteoarthrosis in 11 of 40 rabbit knee joints after meniscal allograft transplantation at 4 to 16 weeks follow-up. Mikic et al.\textsuperscript{50} noted that degenerative changes of articular cartilage in transplanted dog knees were significantly less than those reported after meniscectomy. The degenerative changes that were still present in the transplanted knees were less distinct directly underneath the transplant than in the area not covered by allograft. It was also observed that degenerative changes were less pronounced at 8 and 12 months after transplantation than at 4 and 6 months follow-up, which suggests that articular cartilage may recover over time provided that it is covered by a transplant. On the other hand, Fabriciani et al.\textsuperscript{51} transplanted medial meniscal allografts in goats and demonstrated degenerative changes in both areas of exposed cartilage and the cartilage under the meniscus, and also in the weight-bearing area of the medial condyle at 6 and 12 months follow-up. However, these studies did not grade their observations or did not compare the results with those after meniscectomy. In a semiquantitative study in sheep, Szomor et al.\textsuperscript{28} observed significantly less degenerative changes at 4 months follow-up after both meniscal autograft and meniscal allograft transplantation as compared with meniscectomy. In a comparative study with 6 months follow-up, Jackson et al.\textsuperscript{52} transplanted 10 meniscal autografts, 10 fresh allografts, and 10 cryopreserved allografts in goats with the nonoperated contralateral knee as paired control. A meniscectomy group was not included. On the basis of a grading system, degenerative changes in the transplanted groups were found to be more pronounced than those in
the control knees, but these differences were not significant for each individual group. However, there were significant differences between the degenerative changes in all operated knees together as compared with all control knees. Aagaard et al. found that immediate meniscal transplantation in sheep knees protected the articular cartilage to some extent as determined quantitatively using computer image analysis, at 6 months follow-up. Furthermore, immediate transplantation was superior to delayed transplantation performed at 3 months after meniscectomy.

In clinical practice, second-look arthroscopy has been used for macroscopical analysis of articular cartilage after meniscal transplantation, but until now, this has been done only in a descriptive manner. Van Arkel et al. performed diagnostic arthroscopy before and after transplantation of cryopreserved allografts in 16 patients (10 lateral, 3 medial, and 3 both lateral and medial) at 14 to 55 months follow-up. Fifteen allografts were completely healed to the capsule, 3 allografts were partially detached, and 1 allograft was totally detached. Deterioration of the articular cartilage was not found on the basis of the Outerbridge grading system, nor was improvement in the quality of the cartilage observed after meniscal transplantation. Wirth et al. reported that articular cartilage was more damaged as compared with the preoperative situation in almost all cases at a mean follow-up of 3.8 years after implantation of 14 lyophilized allografts in combination with anterior cruciate ligament reconstruction, whereas 5 patients who had received a deep-frozen allograft showed that the state of the articular cartilage was generally unchanged. Zukor et al. performed a second-look arthroscopy in 8 patients (10 menisci) after transplantation of fresh allografts and noted that the articular cartilage that was covered by the meniscus had a more normal appearance than the rest of the tibial plateau. Finally, Carter reported more degenerative changes of the articular cartilage in 2 of 38 knees at second-look arthroscopy at 24 to 73 months follow-up as compared with the cartilage before transplantation. Both knee joints showed varus malalignment and flattening of the femoral condyle. In summary, it can be stated that degenerative changes of the articular cartilage proceed after meniscal allograft transplantation, although in some studies these changes seem to be less severe on the short term than those reported after meniscectomy.

**Radiographic Evaluation**
The standard evaluation of osteoarthritis in humans includes radiographic examination, although this diagnostic modality is relatively insensitive to early osteoarthritic changes. In a radiographic analysis of rabbit knee joints by Rijk et al., both meniscectomized and transplanted knees showed significantly more osteoarthritic changes in the medial compartment at 1 year follow-up than at 6 weeks after surgery. Statistically significant radiographic differences were not found between the joints that had undergone meniscectomy and those that were subjected to immediate or delayed meniscal transplantation at 1 year follow-up. These results confirmed those of Edwards et
who observed that immediate meniscal transplantation in sheep did not lead to a reduction in osteoarthritic changes when compared to meniscectomy at a mean follow-up of 21.4 months. In addition, meniscal transplantation can even lead to an increase in osteoarthritic changes. In 2 noncontrolled clinical studies, Rath et al.\textsuperscript{14} and Garrett and Stevensen\textsuperscript{60} reported no significant decrease in joint space on 45° posteroanterior weight-bearing radiographs at 2 to 8 years and at 24 to 44 months follow-up, respectively. Ryu et al.\textsuperscript{9} compared preoperative and postoperative radiographs at a minimum follow-up of 2 years after meniscal implantation in 8 patients and found joint space narrowing of 1 to 4 mm in 3 patients, whereas radiographic changes were not observed in 5 patients. Carter\textsuperscript{8} reported progressive degeneration radiographically in only 2 of 38 patients with 46 allografts at a minimum 2-year follow-up after transplantation.

Scintigraphic Results
Bone scintigraphy is a sensitive diagnostic tool for early detection of bone abnormalities in rabbit knee joints.\textsuperscript{61} In a scintigraphic study, Rijk et al.\textsuperscript{62} showed that the protecting effect of immediate meniscal allograft transplantation on articular cartilage against osteoarthritic degeneration is not statistically significant on a long-term basis, whereas delayed transplantation resulted in more degenerative changes of articular cartilage than meniscectomy only.

Histological Evaluation
Two studies in dog knees did not show histological signs of degenerative changes of articular cartilage at 2 and 6 months follow-up after immediate meniscal allograft transplantation.\textsuperscript{2,63} In contrast, Arnoczky et al.\textsuperscript{64} and Mikic et al.\textsuperscript{65} demonstrated degenerative changes of articular cartilage at 6 months after meniscal transplantation in 2 other studies in dogs, but these changes were less distinct underneath the transplants. However, the authors did not grade their observations or compare the results with those after meniscectomy. Szomor et al.\textsuperscript{28} concluded that immediate meniscal transplantation in sheep provides some protection, although not complete, against damage to articular cartilage after meniscectomy on the basis of the histological-histochemical grading system of Mankin et al.\textsuperscript{66} Elliott et al.\textsuperscript{67} observed in a study in dogs significant histological changes in cartilage structure of the medial femoral surface at 3 months after meniscal transplantation that did not differ from changes observed after meniscectomy. Cummins et al.\textsuperscript{58} reported that both immediate and delayed meniscal allograft transplantation in rabbits offer initial protection to the articular cartilage of knee joints at 3 months after transplantation and that delayed transplantation may even reverse initial degenerative changes. However, histological analysis of the articular cartilage in sheep by Aagaard et al.\textsuperscript{69} and in rabbits by Rijk et al.\textsuperscript{70} showed that the protecting effect of meniscus transplantation immediately after meniscectomy is significant on a long-term basis, whereas delayed trans-
plantation results in more osteoarthritic changes than meniscectomy only. These findings suggest that when initial degenerative changes due to meniscectomy are reversed after meniscal transplantation, it is only temporary. To date, no clinical reports have been published evaluating histologically changes of the articular cartilage after meniscal transplantation. It can be concluded that experimental histological studies that investigate the prevention of osteoarthritic changes in meniscectomized knees following immediate or delayed meniscal allograft transplantation are not unequivocal. In general, immediate meniscal transplantation seems to provide more protection of the articular cartilage than delayed transplantation.

**Biochemical Results**

Biochemical changes of articular cartilage after meniscal allograft transplantation mostly have been graded as a part of overall scoring systems without making distinction between individual variables. Recently, Rijk et al. evaluated functional changes in articular cartilage of rabbit knees after meniscectomy with or without immediate or delayed meniscus transplantation by measuring the lactate dehydrogenase activity in chondrocytes as a measure of their vitality and the proteoglycan content of the extracellular matrix as a measure of its quality. Immediate meniscal allograft transplantation did not significantly reduce degenerative changes of articular cartilage at 1 year follow-up when compared with meniscectomy only. Moreover, delayed meniscal transplantation induced even more degenerative changes in the articular cartilage than meniscectomy. Before meniscus transplantation can be considered as an alternative to meniscectomy, further research is required to better assess the biochemical changes in articular cartilage after meniscal allograft transplantation.

**Biomechanical Results**

Long-term protection of articular cartilage by meniscus transplantation may be predicted on the basis of short-term biomechanical studies. Several studies have investigated the effects of meniscus replacement on knee biomechanics and articular cartilage. Bylski-Austrow et al. reported that the decrease in joint pressure at 8 months after meniscal allograft transplantation in goats was not significant when compared with joint pressure in meniscectomized knees, implying that the transplanted menisci had few biomechanical effects. These findings are in agreement with those of Sommerlath and Gillquist who found that a medial meniscus prosthesis did not add much to the compression behavior of a meniscectomized knee. In a dog study, Elliott et al. showed that the tensile modulus of articular cartilage of the femur following either meniscectomy or allograft transplantation was significantly lower than in nonoperated controls. In summary, it remains to be established from a biomechanical point of view whether meniscal allograft transplantation allows for a more equal distribution of weight in the knee joint.
MRI

The role of MRI in the evaluation of degenerative changes in articular cartilage is becoming more and more important. Wirth et al. performed MRI to analyse articular cartilage after transplantation of 3 deep-frozen meniscal allografts and 6 lyophilized allografts in 9 patients at a long-term follow-up. In the deep-frozen meniscal allograft group less degenerative changes were observed than in the lyophilized meniscal transplant group. However, the quality of the MRI scans was not the same for all patients. At present, more sophisticated MRI techniques are available that will allow for more sensitive analysis of articular cartilage after meniscal transplantation in the near future.

Discussion

The meniscus is an important structure for the maintenance of normal joint function and the prevention of cartilage degeneration. The increasing awareness of the consequences of meniscectomy has led to the rationale for investigating meniscal-retaining procedures. Meniscal allograft transplantation may be a good alternative to replace a severely damaged meniscus. Several publications have documented meniscal allograft healing in animal models. However, the ultimate success of the procedure is not whether meniscal allografts can be transplanted into a host knee, but whether the tissue can be made to function and to preserve articular cartilage. While variables such as graft healing, blood supply, cellular repopulation, composition of the extracellular matrix, and structure of the allografts are important, it is not clear how these variables relate to the chondroprotective abilities of transplanted menisci.

Furthermore, animal studies cannot be directly compared with clinical trials because transplantation in animals mostly has been performed immediately after meniscectomy, whereas in humans, transplantation is delayed because the indication for meniscal transplantation is usually symptomatic degenerative joint disease due to meniscectomy. In a histological and histochemical analysis, Rijk et al. showed significant degenerative changes of articular cartilage at 6 weeks after meniscectomy in rabbits. The results obtained after meniscus transplantation in rabbits at this point of time were significantly poorer at 1 year follow-up than those obtained after transplantation performed immediately after meniscectomy. These findings confirm that results obtained after immediate meniscal allograft transplantation differ clearly from results obtained after delayed transplantation. The poor results after meniscal transplantation in rabbit knees with degenerative changes of the articular cartilage are in agreement with those of a clinical study of Garrett who reported a high failure rate in knees with advanced degeneration of articular cartilage at a 2- to 7- year follow-up. It has been suggested that meniscal allografts implanted in arthritic knees fail secondary to abnormal biomechanics, joint surfaces, and destructive enzymes.
A clinical implication of these findings may be that when the aim of meniscal transplantation is to reduce degenerative changes of articular cartilage, it has to be performed as soon as possible after meniscectomy. However, the difficult question in the human situation is how early to consider meniscal allograft transplantation. In the first years after meniscectomy, patients have no symptoms and meniscal transplantation cannot be recommended at present for a patient without complaints. An objective indicator is needed for the detection of early degenerative changes of articular cartilage after meniscectomy before development of significant cartilage injury. Potter et al.\textsuperscript{79} reported that high-resolution MRI allows assessment of early softening and fibrillation of hyaline cartilage. In another study, it was demonstrated that bone scintigraphy also is a sensitive diagnostic modality for detecting early degenerative changes in human knee joints.\textsuperscript{57} However, Rijk et al.\textsuperscript{62,70} found significant degenerative changes in a histological study in rabbit knees at 6 weeks after meniscectomy, whereas scintigraphic changes were not observed at that point of time. It remains to be studied which modality is the most sensitive indicator of early degenerative changes in articular cartilage. In the future, analysis of collagen or proteoglycan breakdown products and proteinase activity in synovial fluid of knee joints after meniscectomy may provide early evidence of cartilage breakdown. Such information may assist in determining the appropriate point in time to consider meniscal transplantation in postmeniscectomy knees.

It remains to be established whether the meniscus must be viable at the time of transplantation or whether it can be nonviable and act merely as a biological scaffold for migrating cells from host tissues. Rodeo et al.\textsuperscript{80} examined biopsy specimens from 28 human meniscal transplants and demonstrated repopulation with cells that appeared to be derived from synovial tissue. Incorporation of the allograft begins at the periphery and progresses towards the center. More research is required to evaluate the significance of these findings for mechanical function of meniscal allografts.

Several studies have assessed macroscopically and microscopically the degeneration of articular cartilage after meniscal transplantation in animal models by using semiquantitative scoring systems in which various histological variables are added to obtain a summed score.\textsuperscript{28,67,68,81} The relative importance of these individual variables in the overall histological score is not apparent a priori. Controlled investigations of structural changes in articular cartilage in human knee joints have even more limitations.\textsuperscript{82,83,84} The development of degenerative changes in human knees can vary widely on the basis of genetic heterogeneity and differences in nutritional, biomechanical, and pharmacological history, all of which can be only incompletely established by epidemiological studies. Furthermore, the lack of sensitive noninvasive methods to identify early disease, the relative inaccessibility of diseased tissues for sampling, and the limitations in obtaining control tissues are obstacles to use human tissues for the study of osteoarthritic changes.

It has been documented that meniscus transplantation in humans may lead to promising improvements in pain, swelling, and knee function.\textsuperscript{13,85} However, most clinical reports have been short-term follow-up studies without control groups. In
addition, pain relief is subjective and the possibility of some placebo effect must be considered. Nevertheless, it may be argued that even short-term improvements in pain and activity levels are successes for some patients, although medical sciences require longer follow-up studies and a larger number of clinical evaluations to establish objectively whether meniscus transplantation is advantageous. Furthermore, clinical results in the literature are difficult to compare because surgical and fixation techniques, additional procedures, preservation techniques, number of patients, and clinical evaluation differ widely and often no distinction is made between medial and lateral meniscal transplantation. Because of anatomical and functional differences between the medial and lateral meniscus, the results obtained after medial meniscus transplantation cannot be compared with those obtained after lateral meniscus transplantation. In a survival analysis, Van Arkel and De Boer\textsuperscript{86} reported significantly different results after transplantation of medial and lateral allografts in humans using the same surgical technique. The minimum requirements for a controlled comparative study in which the issue of meniscal replacement is evaluated with reference to articular cartilage changes must comprise three groups: a replacement group, a meniscectomy group, and a normal or sham-operated control group. Because it is virtually impossible to obtain human cartilage, changes of articular cartilage after meniscal transplantation must be studied in animal models. These models have the advantage of assessing biologic factors after meniscal allograft transplantation by allowing the use of the contralateral knee as a paired control. Rabbit models, for example, have proven to be one of the better models for the human situation because of similarities in histological and biochemical aspects of rabbit and human articular cartilage.\textsuperscript{87,88} Furthermore, osteoarthritis in small animals like rabbits progresses at a faster rate than in larger animals or humans.\textsuperscript{89} Because 1 year can be considered as long-term follow-up in these models, small animals are useful for evaluating late articular cartilage changes on the long term. On the other hand, surgical procedures in small animals such as the rabbit are rather difficult to perform and may introduce artefacts that are hard to interpret when comparing data obtained in small animals with those obtained in larger animals and humans. Although it is usually assumed that the biology of the tissue and the physiology of the biological processes are comparable between commonly used experimental animals, differences in kinematics of knee joint of quadruped animals may introduce different physical forces acting on the meniscus than in humans. Therefore, animals can not be considered to be optimal models for evaluating meniscal transplantation.

Current methods to objectively evaluate meniscal allografts macroscopically after transplantation in humans include MRI and second-look arthroscopy. Potter et al.\textsuperscript{90} correlated MRI findings after meniscal transplantation with clinical, arthroscopical, and histological findings. MRI assessed accurately allograft attachments. Degenerative changes of the allograft were indicated by increased signal intensity. Verstraete et al.\textsuperscript{91} also found a strong correlation between MRI findings and clinical outcome in patients with poor, good, and excellent clinical results, even though MRI cannot be used to predict clinical outcome in every case. However, both studies are descriptive
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without statistical analysis and the observers were not blinded to the results. Van Arkel et al.\textsuperscript{54} reported a better correlation between clinical results and arthroscopy than between clinical results and MRI after meniscal transplantation. It was concluded that the correlation between clinical results, arthroscopy, and MRI could be improved by more sophisticated MRI techniques. Dynamic MRI and weight-bearing MRI may be used in the future to evaluate meniscal allografts.

Aside from these considerations, meniscal allograft transplantation will possibly have to stand the competition of tissue engineering products, collagen scaffolds, and gene therapy on the short term. Implantation of modified mesenchymal stem cells with a gene encoding for bone morphogenetic protein-7 into osteochondral defects in rabbit knees resulted in complete or nearly complete cartilage regeneration at 8 and 12 weeks follow-up.\textsuperscript{92} Furthermore, meniscal tissue obtained by tissue engineering consisting of fibroblasts and chondroblasts seeded on polymer scaffolds has been implanted into partial meniscal defects in rabbit knees and it was found that the reconstructed areas had the same histological appearance as the native meniscus at 1 year follow-up, both in cellularity and organization of collagen fibers.\textsuperscript{77} In the near future, meniscal regeneration will probably combine the improving scaffold technology with gene therapy forming a useful alternative to meniscal allograft transplantation.

Although it has been demonstrated that meniscal allograft transplantation is technically feasible, more research is needed to determine the long-term results. Success of the procedure must not be measured only by healing of the meniscal allograft or short-term relief of pain. Especially, quantitative assessments of the histology and function of articular cartilage are needed to determine objectively whether meniscal allografts are able to exert functions of the native meniscus and prevent cartilage degeneration after meniscectomy in the human knee joint.

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