Meniscal Allograft Transplantation: Updates and Outcomes



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Contents

17.1	Introduction	176
17.2	Graft Procurement	176
17.2.1	Laws and Regulations	176
17.2.2	Donor Selection and Suitability	177
17.2.3	Graft Harvesting	177
17.2.4	Graft Treatment	177

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17.2.5 17.2.6	Graft Storage Sizing of the Meniscus	178 178
		1/0
17.3	Indications for Meniscal Allograft	179
1721	Transplantation	
17.3.1	Indications	179
17.3.2	Contraindications	179
17.4	Preoperative Issues	180
17.4.1	Examinations and Investigations	180
17.4.2	Obtaining a Meniscus Allograft	180
17.5	Surgery	180
17.5.1	Surgical Technique	180
17.5.2	Medial Meniscus Allograft	
	Transplantation: Bone-Plug	
	Technique	181
17.5.3	Medial Meniscus Allograft	
	Transplantation: Soft Tissue	
	Technique with Bone Tunnels	183
17.5.4	Lateral Meniscus Allograft	
	Transplantation: Bone Bridge	
	Techniques	183
17.5.5	Lateral Meniscus Allograft	
	Transplantation: Soft Tissue	
	Technique	185
17.5.6	Lateral Meniscus Allograft	
	Transplantation: Bone-Plug	
	Technique	185
17.5.7	Open Technique for Meniscal	
	Allograft Transplantation	185
17.5.8	Combination with Other Procedures	185
17.5.9	Discussion of Differences	
	Between the Techniques	185
17.5.10	Conclusion	186
17.6	Rehabilitation Following Meniscal	
	Allograft Transplantation	186
17.6.1	Factors Influencing the Rehabilitation	
	Programme	186

17.6.2	Rehabilitation Programme	186
17.7	Outcomes of Meniscal Allograft	
	Transplantation	188
17.7.1	Patient-Reported Outcomes	188
17.7.2	Survival Rates	189
17.7.3	Radiologic Outcomes	189
17.7.4	Return to Sports	190
17.7.5	Complications	190
17.7.6	Conclusion	190
References		

17.1 Introduction

Osteoarthritis after removal of the medial meniscus was demonstrated in dogs in the 1930s [44] and in humans in the 1940s [24]. During the following decades, the important role of the menisci was confirmed in several clinical and experimental studies. The first animal studies on meniscal transplantation were carried out in the 1980s [8, 15]. Milachowski performed the first human MAT in 1994 together with anterior cruciate ligament (ACL) reconstruction in 22 patients from 1984 to 1986. This was an open surgery, and either gamma-sterilized lyophilized or deepfrozen grafts were used, and long-term results were published in 2002 [89]. In Belgium, Rene Verdonk started performing meniscal allograft transplantation in 1989, and his group has published important studies in this field [82, 84–86]. In the Netherlands, Herman de Boer and Ewoud van Arkel have published several studies on the outcome of MAT [77-79]. In the USA, John Garret started with MAT in 1986 [26]. Other important contributors in this field in USA have been Frank Noyes, Robert F. LaPrade, Bill Garret, Steve Arnoczky, Marlow Goble and Brian Cole. In Canada, Allan Gross and John Cameron started early with osteochondral and meniscal allografts [95]. From South Korea a large number of studies have been published [38, 40, 41, 46– 48]. The list of contributors listed here is not complete, and many others have contributed in the evolving research on MAT.

After being originally regarded as experimental surgery, MAT has today become an established treatment method [58]. However, there are no randomized clinical trials (RCTs) or other comparative studies with a control group of conservatively treated post-meniscectomy patients. Several case series have shown good results following the procedure in the short and midterm, while long-term results are not well documented. Particularly, a preventive effect on the development of osteoarthritis (OA) has not been shown. The outcomes are less favourable with increasing cartilage degeneration at implantation, and the availability of meniscal grafts is limited. Proper patient selection is important to obtain optimal improvement in the patient's function and to ensure that the available meniscal allografts are reserved for patients with the highest potential benefit from the procedure. Studies are still lacking to determine the best way to perform graft processing, handling, surgery, and rehabilitation.

17.2 Graft Procurement

17.2.1 Laws and Regulations

The use of musculoskeletal tissue from donors for transplantations is regulated in detail in the USA and in Europe. In the USA, the Food and Drug Administration (FDA) sets the requirement for the tissue banks: All tissue banks have to be registered with the FDA, donor testing must be performed by screening and testing for communicable diseases and current good practice must be followed during the tissue processing (Food and Drug Administration 21 CFR Parts 207, 807, and 1271). In addition to the FDA regulations, the American Association of Tissue Banks (AATB) has accredited most of the musculoskeletal tissue banks in the USA. AATB has established further recommendations for the handling of allograft tissue (AATB Standards for Tissue Banking 14th Edition).

In the European Union (EU), the use of musculoskeletal tissue for transplantation is regulated by the European parliament through EU directives. However, national regulations may differ from these. The European Council representing 47 countries and the WHO have also provided guidelines for tissue transplantations, and national and international association of tissue banks all over the world has their own guidelines and ethical rules.

17.2.2 Donor Selection and Suitability

17.2.2.1 Eligibility

The first step in the process is to obtain consent from the potential donor's family. Most European countries have developed a so-called presumed consent from the donor, but require an additional consent from the family. In the USA persons who want to become donors provide their written consent before death. The next step is to assess the suitability of the donor. This includes a medical history where systemic autoimmune diseases, neurological disorders, genetic diseases, chronic infection, alcoholism and malignancy are general contraindications. There is no upper age limit regulated by law. The European guidelines have an upper age limit for meniscal allografts of 45 years. One US tissue bank (Joint Restoration Foundation) uses only donors under 35 years for meniscal allografts.

17.2.2.2 Physical Examination

A physical examination of the donor is an important step to identify donors with an increased risk for transmitting disease. Five percent of donors are excluded at this step.

17.2.2.3 Testing

The minimum requirements for biological tests of the donor include anti-HIV-1, anti-HIV-2, NAT HIV, HBs Ag, total anti-HBc, antibodies to HCV, NAT for HCV, antibodies to HTLV types I and II and syphilis which all must be negative for the donor tissue to be released.

17.2.3 Graft Harvesting

17.2.3.1 Time Limits

In the USA harvesting must be performed within 24 hours if the body has been cooled and within 15 hours if not and in Europe within 12 hours without cooling and 48 hours with cooling.

17.2.3.2 Facilities and Personnel

Graft harvesting should be performed in an aseptic environment. The handling personnel must have the appropriate training. Sterile draping and instrumentation must be used. After opening the knee, the menisci are inspected for damage. If suitable for transplantation, the meniscus is taken out with 2–3 cm section of the corresponding tibia plateau. The graft must be wrapped in an aseptic way and transported to the tissue bank. In the USA, further processing before freezing must be completed within 72 h.

17.2.4 Graft Treatment

17.2.4.1 Primary Processing of the Meniscal Allograft

The tissue must be tested for bacterial contamination by culture. Further processing includes physical debridement, mechanical agitation, ultrasound processes, alcohol solutions, rinses and antibiotic treatment [53] with the aim to remove blood and lipids and minimizing the risk for disease transmission and immunological reactions.

17.2.4.2 Graft Sterilization

All allografts have a potential for disease transmission, but the risk for transmission has been estimated to be very low, with between 1 in 173,000 and 1 in 1 million for HIV and 1 in 421,000 for hepatitis C for unprocessed grafts [53]. Different methods have been investigated to minimize this risk without hampering the properties of the graft. Cells will be destroyed by such methods, so fresh viable grafts and cryopreserved grafts are not sterilized.

Gamma radiation at 2.5 mrad or higher has been shown to negatively affect the biomechanical properties of menisci [90, 91]. It has been debated whether a lower dose could give sufficient sterilization with no or acceptable harm to the tissue. A recent experimental rabbit study showed a negative effect also with 1.5 mrad on scanning electron microscopy, but no difference in histology compared to non-radiated grafts [94]. Ethylene oxide has been shown to induce a persistent synovitis [32] and is not currently used. Peracetic acid sterilization has also been used but has been shown to harm the biomechanical properties and inhibit remodelling of ACL grafts in an animal model [66]. The same has been demonstrated for electron beam radiation which has been proposed as an alternative to gamma-radiation [67].

In summary, all secondary sterilization methods with sufficient virucidal and bactericidal effects are harmful to a meniscal allograft. Secondary sterilization is therefore no longer used by most tissue banks.

17.2.5 Graft Storage

There are four methods for graft storage: fresh viable grafts, cryopreserved grafts, lyophilized grafts and fresh-frozen grafts. The latter is the graft most commonly used today.

17.2.5.1 Fresh Viable Grafts

These grafts contain viable cells which in theory would be an advantage [83]. However, clinical studies have not reported better results with these grafts. Harvesting must be performed as soon as possible (varying from 4 to 12 h according to different authors). The graft must be kept at 4 °C for 10–14 days in the patient's serum while necessary donor testing and planning are performed. This short time frame poses a challenge in finding a suitable recipient and transporting of the graft to a distant hospital if needed. The risk of disease transmission is also regarded as higher compared to other methods.

17.2.5.2 Cryopreserved Grafts

With this technique the graft is immersed in a cryoprotective agent (usually glycol), a culture medium and an antiseptic agent. The graft is then slowly cooled to -196 °C. The cryoprotective agent stops the formation of ice crystals, and the grafts have been reported to have viable cells after thawing. The collagen network seems to be better preserved with this technique. However, the method is quite complicated and costly. Experimental [23] and clinical outcomes [30] have not been reported to be better with this method compared to others, and the method is little used today.

17.2.5.3 Lyophilization

This is a so-called freeze-dried meniscus. The tissue is frozen in a vacuum and dehydrated. The graft is thawed and rehydrated before implantation. It can also be stored at room temperature and the process allows long storage. There may be a negative effect on biomechanical properties [27], and clinically there seems to be a higher risk for effusion and synovitis [57]. Of note, this method is no longer used.

17.2.5.4 Fresh-Frozen Grafts

This is by far the most common method to store meniscal allografts today. The method is simple and possibly less immunogenic. After the initial processing, the graft is quickly frozen to -80 °C. Donor cells are destroyed by the freezing process. Grafts can be stored for up to 5 years. The lack of viable cells has not been reported to have a negative effect on the clinical outcome. The graft must be transported from the tissue bank to the implanting hospital as fast as possible in insulating package while keeping the graft frozen. At arrival the graft must immediately be placed and kept in a freezer at -40 °C or below until implantation.

17.2.6 Sizing of the Meniscus

17.2.6.1 Sizing of the Donor Meniscus

During the initial processing of the meniscus, the anteroposterior and mediolateral distances are measured. These are the most important measurements. In addition, the width of the meniscus itself at the anterior, middle and posterior parts can be measured (not all tissue banks do this).

17.2.6.2 Sizing of the Recipient

Several methods have been proposed for best possible sizing of the recipient. The sizing can be based on plain radiographs, CT, MRI of the same or contralateral knee or anthropometric measurements. Radiographs must have a calibrating sphere or a similar marker to obtain correct measurements. According to Pollard's method, the distance between a vertical line lateral/medial to the tibial eminence and a vertical line at the lateral/medial margins of the tibial plateau is measured in the coronal plane and the anteroposterior distance between a vertical line at the tibial tuberosity and the posterior tibia plateau in the sagittal plane. The width of the meniscus in the coronal plane corresponds to the measured distance, while the length of the meniscus in the sagittal plane is 80 % of the measured distance for the medial meniscus and 70 % for the lateral meniscus [62]. Yoon et al. found that this method overestimated the anteroposterior length of the lateral meniscus and suggested another formula: $0.52 \times$ Tibia AP length (in mm) + 5.2 mm [92]. The measurements for the Pollard method can also be obtained with more exact results by CT scan but includes a higher radiation risk. MRI is regarded the gold standard and is widely used. Using MRI of the contralateral knee has also been advocated [93]. Van Thiel has recommended the use of the patient's gender, weight and height in a formula to estimate the size of the meniscus [81]. In a recent article by Yoon's group, they concluded that MRI is the best option to size a meniscus transplant graft. For the lateral side of the knee, anthropometric measurements according to van Thiel is an alternative, while the Pollard method is an alternative on the medial side [34].

17.3 Indications for Meniscal Allograft Transplantation

17.3.1 Indications

The ideal candidate for meniscal allograft transplantation is a patient with a painful knee following a total or subtotal meniscectomy with no symptoms of instability and with normal cartilage and normal alignment. The symptoms should be severe enough to justify a large operation with potential complications, including the risk of an inferior result. This usually means that the patient should have pain during daily activities and pain making sport activities impossible or difficult. In addition, the symptoms must correspond to the clinical findings, i.e. in the case where the medial meniscus has been resected, the symptoms should be located to the medial joint line. Other symptoms may be swelling or locking. The duration of symptoms should be of at least 6 months. The patient must be willing and

capable to follow the rehabilitation programme following surgery. The patient should also do "prehab" which means training of knee function before surgery, preferably guided by a physiotherapist with the necessary knowledge and interest. This will make him/her better prepared for surgery, and in some cases the patient will improve so well that MAT may no longer be indicated at that point in time.

When there are cartilage injuries/defects present, MAT may still be indicated, but the prognosis is somewhat less favourable with a higher failure rate, and the patient needs to be informed about this [36]. In the authors' opinion, one can accept quite severe cartilage changes in a young patient, but should be more "strict" in patients over 40 years of age.

In the case of varus alignment in a medial meniscus-deficient knee, a valgus high tibial osteotomy is preferred as the first-line treatment. In most cases, this will relieve symptoms enough so a later MAT is usually not needed. Similarly, in the case of valgus alignment in a lateral meniscus-deficient knee, a distal varus osteotomy of the femur is usually the first treatment of choice, or it can be performed concurrently [45]. Some authors perform HTO together with MAT [35, 36, 85].

In cases of instability, this is usually corrected before or concurrent with a MAT. In failed ACLreconstructed knees with deficient medial meniscus and no other obvious causes of graft failure, a concomitant ACL revision and medial MAT may be indicated.

17.3.2 Contraindications

MAT is usually not indicated in patients over age 50, although case series of MAT including patients in this age group have been reported [74]. In many patients over 40, there will be degenerative changes that contraindicate a MAT. Kellgren-Lawrence grade 2 and more (osteophytes and joint space narrowing) are also contraindications. Other contraindications are signs of infection, inflammatory joint disease and BMI above 35 [14].

17.4 Preoperative Issues

17.4.1 Examinations and Investigations

The first step is to obtain a thorough history from the patient. When did the injury occur? What are the symptoms today? What can the patient do and what can he/she not do? It is very important to ask the patient what he/she wants to do and what his/her expectations following surgery are. If there is a discrepancy between the patient's expectations and what can be obtained with surgery, it is very important to help the patient to have realistic expectations, by providing thorough information. Previous surgical reports from other hospitals should be collected. The patient should fill in an appropriate patient-reported outcome measures (PROMs) like Lysholm score, Cincinnati score, KOOS score, or others. An activity score like the Tegner score or similar should also be used. This will help in the preoperative evaluation of the severity of the symptoms, will help in the decision for surgery, and can be compared with post-operative scores at a later stage as part of the quality control of the results of MAT in the institution.

The clinical exam must include a thorough inspection of the limb axis, gait and other factors. The knee is inspected for swelling and muscle atrophy and examined for laxity, direction of possible laxity and tenderness, particularly along the joint lines. All patients where MAT is considered should have standing x-rays with 30° of knee flexion to evaluate the joint space and osteophytes. Long-standing radiographs from the hip to ankle with extended knees should be obtained to evaluate alignment. Recent MRIs should be evaluated or new MRIs obtained to evaluate the status of the menisci, cartilage, ligaments and other structures. The authors prefer in most cases to perform a diagnostic arthroscopy to obtain a complete status of the knee to confirm that the meniscus status is not better than anticipated and that the condition of the cartilage and ligaments does not contraindicate a MAT before a meniscus allograft is ordered from the tissue bank.

17.4.2 Obtaining a Meniscus Allograft

For most surgeons a fresh-frozen meniscus allograft is ordered from a certified tissue bank. The surgeon should have good knowledge about their tissue bank, the procedures around the harvest of the graft and how the graft is processed, stored and transported. He/she should also have good knowledge of the rules and regulations related to tissue transplantation. The sizing of the graft is based on MRI or radiographs with a size marker [69, 93]. This is usually done by the tissue bank. Once the tissue bank has a meniscus of suitable size for the patient, an offer is sent to the surgeon. The surgeon should check and compare the given measurements of the donor graft and the recipient, verify it is the correct side and then accept or not accept the graft. Usually a size mismatch up to 5 % is regarded as acceptable [93]. Once the graft is received, the identification should be checked and the graft stored at -40 °C or below until implantation.

17.5 Surgery

The surgery is usually performed under general anaesthesia. Epidural or peripheral (femoralischial) nerve blocks are often used in addition for post-operative pain control. The leg is draped in a standard fashion for knee surgery. Some surgeons prefer a Gilchrist holder around the thigh with a hanging lower leg; others place the leg on a flat table with a foot support and side support to the lateral side of the thigh. A tourniquet may be used to control bleeding. Systemic prophylactic antibiotics are administered to the patient intravenously according to the local recommendations for the hospital.

17.5.1 Surgical Technique

Many different techniques have been described for MAT. Open, arthroscopic and partly open/ partly arthroscopic methods are used. Bony or soft tissue fixation is used with or without bone tunnels. There are no RCTs or other studies that have shown that one technique is superior to others. Therefore, the technique will be the preferred choice of the surgeon, often with personal modifications. Most surgeons would start the procedure with an arthroscopic examination of the knee. Then the remnants of the meniscus are removed by a basket punch and/or shaver. It is important to preserve the outer fibrous rim to maintain the "barrel band" function of the meniscus.

17.5.2 Medial Meniscus Allograft Transplantation: Bone-Plug Technique

17.5.2.1 Graft Preparation

The graft comes with the meniscus attached with its posterior and anterior roots to the tibial plateau bone block. This technique, with small variations, has been described by several authors [1, 21, 39, 42, 45]. The bone blocks are prepared by drilling a pin through the bone block exiting through the meniscal root attachments. Then a collared guide pin (Fig. 17.1) is inserted into the hole created by the pin which is then over-drilled with a 9 mm coring reamer to prepare the two bone plugs. The plugs should not be too long, with the posterior bone plug around 8–10 mm in length to facilitate the later intro-

duction into the joint. Non-absorbable sutures are placed in the posterior and anterior root and through the central pin hole in the bone blocks. Sutures are also placed in the posterior and anterior part of the meniscus (Fig. 17.2). The authors prefer 4 non-absorbable vertical sutures in the posterior part and anterior part, each 5 mm apart. This leaves a part in the middle without sutures. Usually the meniscal allograft is immersed in an antibiotic bath or swab. The type of antibiotics should be selected in cooperation with local microbiologists/infection specialists.

17.5.2.2 Placement of the Meniscus Allograft

Using arthroscopic technique, the posterior root attachment site is visualized. Careful use of shaver, radiofrequency and a mini "notch plasty" under the PCL can create the necessary space and visibility. Perforating the MCL with a needle while holding a valgus pressure can open up the medial compartment slightly and thereby increase visualization and enhance access. The posterior tunnel is drilled by placing an ACL-tibial guide (or similar specially designed "meniscal root" guides that are available) at the posterior root attachment, drilling a guide pin, and a 9 mm tunnel is drilled over the guide pin. A small longitudinal arthrotomy is made medial to the patellar tendon continuous with the medial arthroscopy portal. The ante-

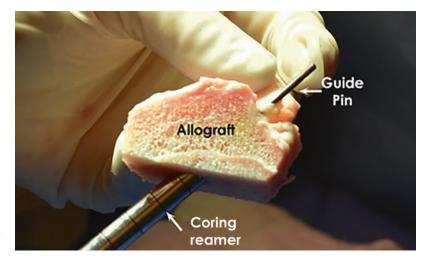
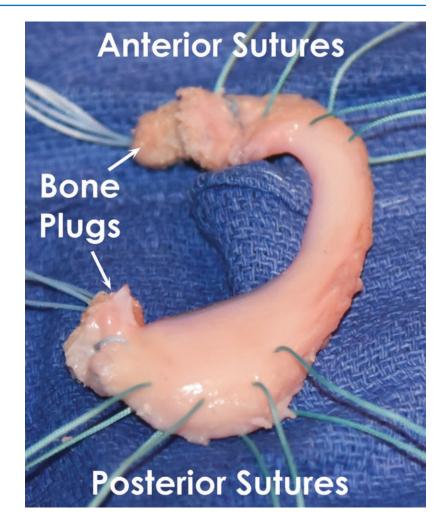


Fig. 17.1 Figure showing the creation of bone plug using a coring reamer over a collared pin



rior root attachment is exposed, and an 8 mm blind tunnel is drilled over a guide pin placed central in the root attachment. Usually, this tunnel is reamed after the MAT is placed into the knee in case the native root attachment location does not precisely match the MAT. By the use of a drill or awl, a small canal from distal and into the bottom of this tunnel is created for the passage of sutures. A posteromedial longitudinal incision is made and the posteromedial capsule is exposed by creating a space between the medial gastrocnemius muscle and the capsule. A spoon or similar instrument is used to protect the posterior structures. Four passing sutures are passed from inside in the posterior part of the joint space corresponding to the sutures placed in posterior part of the allograft, through the capsule and out in the posteromedial incision using a clamp or a suture passer. Then the meniscus graft is introduced into the joint by first pulling the posterior sutures through the bone tunnel and the posterior capsule with the first placed passing sutures. Numbered hemostats can facilitate future tying of the sutures. Then the meniscus is gently pulled in place. The insertion of the posterior bone plug into the tunnel may be facilitated by the use of a hook or a grasper. The anterior bone block is inserted into the anterior tunnel. The sutures are tied against the

Fig. 17.2 Medial meniscus allograft with bone plugs and sutures placed in posterior and anterior horns capsule posteriorly. The anterior part of the meniscus is sutured to the anterior capsule by open surgery with free needles. The sutures from the bone blocks are sutured over a button or the bone bridge between the tunnels. Finally, the middle part of the meniscus without preplaced sutures is sutured by vertical mattress sutures with inside-out sutures with long needles.

17.5.2.3 Variations of This Technique

Some surgeons use one bone plug in the posterior end and only soft tissue in the anterior end. This will allow for adjustment of the meniscus tension in cases of size mismatch [51, 76]. The suture placement can also vary. Some use fewer preplaced sutures in the graft and more inside-out sutures after placement of the graft. Some surgeons use all-inside suture systems [4]. The external tunnel opening in the tibia can be anteromedial or anterolateral depending on the surgeon's preference. The bone plugs may also be created with the use of other techniques.

17.5.3 Medial Meniscus Allograft Transplantation: Soft Tissue Technique with Bone Tunnels

In many of the steps, this method is similar to the bone-plug technique [1, 6, 65, 72]. When using only the meniscus root attachments without bone, it is important that these attachments in the allograft are well preserved and of good quality. The sutures need to be placed in a fashion to ensure a secure hold in the anterior and posterior roots of the meniscus. According to surgeons using this technique, this allows for adjusting the tension/outer diameter of the meniscus to fit with the condyles. With this technique the meniscus can be introduced into the joint through a smaller opening without an arthrotomy.

17.5.4 Lateral Meniscus Allograft Transplantation: Bone Bridge Techniques

The root attachments of the lateral meniscus are very close to each other. By keeping the roots of the allograft attached to a bone bridge, the correct distance between these attachments can be maintained with the root attachments connected by the bone block. As with a medial MAT, the first part of the operation is a diagnostic arthroscopy, followed by removal of meniscus remnants with care to preserve enough of the outer fibrous rim. The bone bridge technique with variations has been described by several authors [17, 43].

17.5.4.1 Graft Preparation

With the dove tail technique [17], the bone block is prepared by the use of a specially designed cutting system (Fig. 17.3) creating a trapezoidshaped (viewed in the anterior-posterior direction) bone block. The block is trimmed so that it fits into the corresponding "sizer" (Fig. 17.4). Sutures are placed in the meniscus substance in the similar way as in the bone-plug technique above.

17.5.4.2 Placement of the Meniscus Allograft

A posterolateral longitudinal skin incision is made just posterior to the fibular collateral ligament (FCL), the iliotibial tract is opened in the direction of the fibres and the capsule is exposed by creating a space between the capsule and the lateral gastrocnemius muscle. A spoon or similar instrument is placed between the capsule and the posterior structures to protect the neurovascular structures. Four passing sutures are placed in the same way as described for the medial side boneplug technique.

An anterolateral arthrotomy is performed through an incision lateral to the patellar tendon as an extension of the lateral arthroscopy portal.

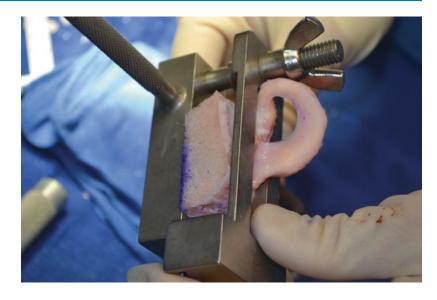
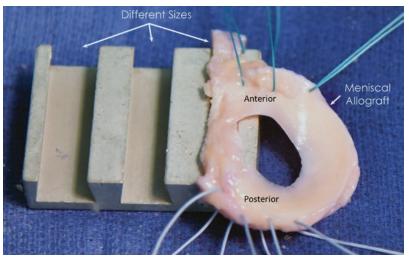


Fig. 17.4 Measurement of bone block of lateral meniscal allograft. Three sutures (*green*) have been placed through the anterior horn and four sutures through the posterior horn



A similarly trapezoid-shaped trough is created in the tibia in the anterior-posterior direction through the root attachments. This is done by first removing the protruding tibial spine between the roots and then tapping in a chisel with a guide pin on top to achieve the correct depth. The rest of the remnant bone in the trough is removed first by drilling and then shaped by the use of trapezoidshaped rasps of similar size as the bone block. The posterior cortex of the tibia is preserved. The meniscus is introduced by first pulling the preplaced sutures in the posterior part of the meniscus through the capsule, then passing the bone block into the trough and simultaneously pulling gently in the sutures till the meniscus is in place. With a bone block that fits well into the trough, the bloc will now be stable. The sutures are tied and placed in the same fashion as for the medial meniscus bone-plug technique.

17.5.4.3 Variations of This Technique

Some authors prefer a rectangular-shaped bone block and securing the block with sutures in the anterior and posterior end through bone tunnels [68]. A technique using an interference screw for fixation of the bone block has also been described [25]. With these techniques the stability of the bone block is less dependent on an exact fit into the trough.

cutting

Fig. 17.3 Lateral meniscus allograft bone block in work station for

17.5.5 Lateral Meniscus Allograft Transplantation: Soft Tissue Technique

Several authors have published the use of soft tissue fixation of the anterior and posterior horns through bone tunnels and suturing the meniscus to the capsule as described for the medial meniscus soft tissue technique [2].

17.5.6 Lateral Meniscus Allograft Transplantation: Bone-Plug Technique

Lateral MAT is most commonly performed with a bone bridge or soft tissue fixation of both horns in tibial tunnels. The proximity of the root attachments makes it difficult to use two bone plugs, but this technique has been presented by some authors [2].

17.5.7 Open Technique for Meniscal Allograft Transplantation

Meniscal allograft transplantation started with an open technique in the 1980s, but is now less common. For the both lateral and medial side, an arthrotomy is performed with bony detachment of the ligamentous complex from the femur for access. The detached ligament with bone is refixated to the femur at the end of the procedure. Soft tissue fixation of the anterior and posterior horns can be performed with sutures through tibial tunnels [22, 87] or with fixation of the roots to the remnants of the original meniscal root attachments without tunnels [85].

17.5.8 Combination with Other Procedures

MAT can be performed in combination with other procedures in the same knee either concomitantly or as a separate procedure. The most common procedures are ACL reconstruction, ACL revision and tibial or femoral osteotomy. In selected cases cartilage procedures as autologous chondrocyte implantation or osteochondral transplants can be performed. Describing these techniques is beyond the scope of this chapter.

17.5.9 Discussion of Differences Between the Techniques

As mentioned, there are no RCTs comparing different techniques, and the preferred technique will be the personal preference of the surgeon with soft tissue techniques usually regarded as quicker and easier to perform. However, there are some issues to be discussed regarding choice of technique.

17.5.9.1 Clinical Outcome

Most published studies in clinical outcome are case series with no control group. In general, the clinical outcome using PROMs is good both in the short and midterm for all techniques. In a study of patients with lateral MAT, patients with a graft fixed with the bone bridge technique had significantly better range of motion compared with patients having the graft fixed with soft tissue sutures in bone tunnels [68].

17.5.9.2 Graft Extrusion

Graft extrusion means that the implanted meniscus is displaced externally leaving more of the joint surface exposed. This will in theory increase the risk for later OA, but a negative effect of extrusion on clinical scores has not been demonstrated to date. One study compared bony versus soft tissue fixation in bone tunnels and found no difference in clinical outcome, but more graft extrusion in the soft tissue group [1]. Another study showed a higher extrusion rate in patients treated with an open technique with soft tissue fixation without bone tunnels compared to arthroscopic soft tissue fixation in bone tunnels [20]. In a multivariate study of graft extrusion in a series of lateral MAT with bone bridge technique, significant risk factors for the major graft extrusion (more than 3 mm) included delayed time from previous meniscectomy to MAT and increased axial plane trough angle measured on MRI [3].

17.5.9.3 Radiological Outcome

In the prospective study by Abat et al. [2], there was no significant difference in radiological outcome regarding joint space narrowing between the bone-plug group and the soft tissue fixation in bone tunnel group at mean 5 years.

17.5.9.4 Complications, Failures and Reoperations

The same study by Abat et al. reported 33 % complications and 9 % failure rate in the soft tissue fixation group and 16 % complications and 3.6 % failures in bone-plug group [2].

17.5.9.5 Experimental/Biomechanical Studies

Some studies have reported that bone-plug fixation in tunnels restores tibial contact pressure better than soft tissue fixation in bone tunnels or with a bone bridge [7, 19]. In a later similar study, only a slight advantage for the bone plugs on contact pressure was found [54]. In a study of pullout strength, no difference was found [31].

17.5.10 Conclusion

Medial meniscal allograft transplantation is today most commonly performed with two bone tunnels with either soft tissue fixation or bone plugs. On the lateral side, the most common technique is either a bone block connecting the anterior or posterior horns or soft tissue fixation in two bone tunnels. No technique has been shown to be superior regarding clinical outcome. Soft tissue fixation seems to give more extrusion of the meniscus than bony fixation in post-operative MRIs.

17.6 Rehabilitation Following Meniscal Allograft Transplantation

The aim of the rehabilitation is to get the patient as soon as possible back to his/her preinjury functional level without compromising the healing of the implanted graft.

17.6.1 Factors Influencing the Rehabilitation Programme

Animal studies have demonstrated that vascular ingrowth in an injured native meniscus is impaired by immobilization and that early mobilization leads to a stronger repair tissue [13]. Clinical studies support these findings [55, 70]. In a sheep study, Milachowski showed complete healing of lyophilized and fresh-frozen meniscal allografts at 48 weeks with remodelling occurring only in the lyophilized menisci and less vascular ingrowth occurring in the fresh-frozen menisci [57]. Fresh and cryopreserved meniscal allografts in a goat model showed peripheral healing, revascularization, cellularity and incorporation at 6 months [33]. From these studies we can assume that complete healing of a human meniscus allograft may take between 6 months and 1 year.

Both the peripheral capsular fixation and the meniscal root fixations are at risk for reinjury postoperatively. Weight bearing with an extended knee imposes load on the meniscal roots which increases through flexion up to four times at 90° of knee flexion [9]. In open kinetic chain exercises, high tibial contact forces have been estimated [56]. Repetitive low loading of meniscal transtibial root repairs has been reported to increase displacement of the repaired roots [63]. Applying moderate tensile forces at repaired medial meniscal roots has been reported to easily reach a magnitude that exceeds the strength of fixation [73].

These and other biomechanical studies support that rehabilitation following MAT should include restricted weight bearing, restricted ROM and restricted use of open chain exercises. Even though a high risk of allograft loosening may be feared from these experimental studies, the clinical experience is that a total loosening of an implanted meniscal allograft is rare. However, extrusion, which is common, may be a result of displacement of the meniscal root fixation.

17.6.2 Rehabilitation Programme

Rehabilitation programmes have traditionally been divided into phases.

Rehabilitation protocols following orthopaeinterventions are progressed dic through sequenced phases and include active interventions aimed at addressing body impairments and functional limitations [11]. The primary aim is to timely progress the patient towards participation in their desired physical activity and sport, while simultaneously protecting the healing tissue from premature overloading. Current orthopaedic post-operative rehabilitation is progressed through the different phases based on sound clinical reasoning, sequenced functional achievements and the completion of functional milestones. At the same time, knowledge on tissue-specific biologic healing processes must be respected and will guide the early timeline of advancement [28]. Four rehabilitation phases are traditionally outlined:

- The acute post-operative phase aiming at minimizing impairments
- 2. The rehabilitation phase aiming at restoring normal activities of daily living
- 3. The return to sport phase aiming at resuming desired sports activities
- 4. Prevention of reinjuries:
 - Most surgeons performing MAT recommend a rehabilitation protocol in line with the following restrictions [45] with some local modifications. Toe touch weight bearing in a brace locked in extension for the first 6 weeks with gradual transmission to full weight bearing from week 6 to 8.
 - Straight leg exercises in the brace are allowed from day 1.
 - The knee brace is locked the first week. From week 1 to 3, passive and active flexion and extension exercises without external load are allowed as tolerated between 0 and 90 degrees. From week 4, gradual increase to full range of motion is encouraged without application of external force.
 - Cycling is initiated after 8 weeks provided unrestricted knee flexion of 100°.
 - No open chain muscle strengthening exercises before 3 months after surgery.
 - No running or other activities with impact before 6 months after surgery.

 Activities involving pivoting motions and pivoting sports are generally advised against and should under no circumstances be initiated before 9 months after surgery.

Rehabilitation following a MAT first and foremost consists of a targeted exercise programme. Phase 1 is prolonged compared to most other surgical procedures due to restricted weight bearing and ROM. The principles within the acronym POLICE (protection, optimal loading, ice, compression and elevation) are primary tools following any orthopaedic surgical procedure [12]. However, exercise therapy has effects both at a local tissue level and in the central nervous system and should be used as a direct tissue healing stimulation (mechanotherapy) [37]. Concurrently, general conditioning and optimization of function within the allowed load and movement limitations is performed. Patients are guided by physiotherapists to perform daily home-based exercises involving isometric muscle activation and active low-load ROM mobilization exercises. Restoring passive and active knee extension is imperative during this phase. Electrical neuromuscular stimulation is frequently administered to enhance active muscle contractions. Active rehabilitation exercises are often supplemented with medical and manual therapies that may enhance the effects of exercise through pain management and improved tissue adaptations. The success of rehabilitation is dependent on introducing the most effective intervention at the correct time in adequate dosage [11].

In Phase 2 of the rehabilitation, the focus will shift from joint and muscle impairments to gradually increase the complexity of movements from single joint controlled actions to more complex tasks, including movements through several biomechanical planes. During the initial full weightbearing period, the programme will mainly incorporate elements to improve motor control and muscle strength [61]. Specifically, exercises to regain motor control of weight-bearing singleleg stance and terminal knee extension $(0-20^\circ)$ are emphasized to facilitate normalization of walking. Furthermore, quadriceps and hamstring muscle strengthening is focused in combination with gluteal and adductor closed chain exercises. Additional sessions of no-impact cardiovascular training should be incorporated to continue healing of the implanted tissue, with the additional benefit of an increased fitness level.

For a large proportion of patients undergoing a MAT procedure, returning to high-impact or pivoting sports is not realistic [60]. Most patients will experience the short- and long-term benefits of symptom relief and improved function in activities of daily living. However, some may improve substantially and want to pursue highimpact and/or pivoting sport activities. Then, more traditional strength and conditioning training will be incorporated in the weekly rehabilitation programme. The focus on more complexity, velocity and jumping and landing tasks will increase. A higher rate of force development and introduction of sport-specific exercises is emphasized with a gradual progression into on-field training. However, close monitoring of residual symptoms such as joint effusion and/or pain must be continued. Reappearance of symptoms should lead to a discussion on abandoning the aim of resuming strenuous sport activities, which in itself may be the most important action for prevention of a failed meniscus allograft (Phase 4).

17.7 Outcomes of Meniscal Allograft Transplantation

The role of the meniscus in joint preservation, load distribution, lubrication and kinematics has been thoroughly studied [49, 50. 591. Meniscectomy is reported to increase contact pressures in the condyles by 235 % and partial meniscectomy increases condyle pressures by 165 %. Increased contact pressures and joint instability have a negative effect on the longevity of the knee joint. In recent years there has been an increasing interest in meniscus preservation procedures. Despite improved techniques, the meniscus is not always amendable to repair, and hence a meniscectomy is inevitable.

Meniscus allograft transplantation has been introduced to address the problems associated with meniscectomy. Several studies are published on the outcomes of meniscal allograft transplantation (MAT), but most studies are of low quality (retrospective studies with few patients). In a systematic review by Rosso et al. [64] considering 55 articles, none of the studies were level 1, 2 studies were level 2, 7 as level 3 and 46 as level 4. The mean Coleman methodology score of the 55 included articles was 49.7 (24–81). The reported clinical outcomes using patient-reported outcomes (Lysholm, Tegner, IKDC), return to sports and activity after MAT, radiographic outcomes and complication will be discussed.

17.7.1 Patient-Reported Outcomes

Several knee scoring systems are reported in the literature including the Lysholm score, Tegner, visual analog scale for pain and/or overall knee function, International Knee Documentation Committee (IKDC) subjective and objective forms, Knee Injury and Osteoarthritis Outcome Score (KOOS), Short Form-12 (SF-12) or SF-36, Noyes sports and symptoms score, the modified Cincinnati score, the Fulkerson knee score, the Hospital for Special Surgery score, the Western Ontario and McMaster Universities Osteoarthritis Index 7 (WOMAC), the Knee Assessment Scoring System and the Knee Outcome Survey.

Rosso et al. [64] reported in a recent systematic review that the knee function evaluated by the weighted average Lysholm score improved from 55.5 \pm 2.1 to 82.7 \pm 2.7 and the weighted average pain VAS decreased by 4 points from 6.4 ± 0.4 to 2.4 ± 0.4 . All studies reported an improvement at follow-up, suggesting good clinical outcomes at short-term to midterm follow-up. In their systematic review of the 18 studies that compared outcomes for medial and lateral MATs, there were no significant differences except in two studies that reported shorter survival for medial MAT. There was no significant difference between isolated MATs and MATs combined with other procedures and between fixation methods (soft tissue vs. bone block). Some authors have reported an increased risk of meniscal extrusion with soft tissue fixation [1].

In a recent systematic review, Smith et al. evaluated outcomes after MAT in 35 studies including 1332 patients (1374 knees) with a mean follow-up of 5.1 years [71]. The mean Lysholm score improved from 55.7 to 81.3, IKDC scores from 47 to 70 and Tegner activity score from 3.1 to 4.7. A Lysholm score of 65–83 is defined as fair [75]. In the same systematic review, Smith et al. [71] reported failure rates of 10.6 % at 4.8 years and complication rates of 13.9 % at 4.7 years.

17.7.2 Survival Rates

Verdonk et al. reported a survival time of 11.6 years using the cumulative Kaplan-Meier survival rate in 100 patients treated with MAT [85]. There was no difference in failure rates between the medial and lateral meniscus. Failure rates have been reported to increase with time, with van der Wal et al. [80] reporting a 52 % survival rate at 16 years. There are conflicting results on the success rate and survivorship depending on the side. Verdonk et al. reported a cumulative 10-year survival rate of 74 % for the medial side and 70 % for the lateral side [85]. However, van Arkel et al. [78] reported higher success rates for the lateral side (88 %) compared to the medial side (63 %) in a follow-up of 63 patients with a mean follow-up of 60 months.

17.7.3 Radiologic Outcomes

Smith et al. reported a weighted mean joint space narrowing of 0.032 mm across all studies at a mean follow-up of 4.5 years in their recent systematic review. These changes were not significant. Most studies report meniscal extrusion on MRI, but the correlation of meniscal extrusion to clinical outcomes is not clear. Most studies report no correlation, but Yoon et al. found an association between meniscal extrusion and Lysholm score. The grading of meniscal extrusion differs between studies. While some studies report the relative percentage of extrusion of the meniscus allograft extending beyond the edge of the tibial plateau, some studies report absolute measurement of extrusion in millimetres. Some studies use the 3 mm cutoff to describe extrusion, with <3 mm defined as minor extrusion and >3 mm as major extrusion. Regardless of the grading system, most studies report meniscal extrusion on MRI follow-up. There are conflicting reports in the literature on which meniscus allograft has a high risk of extrusion (medial vs lateral), but there seems to be no significant difference. Only a few studies have evaluated the progression of meniscal extrusion on MRI over time. Verdonk et al. [86] reported progressive meniscal extrusion from 1 year to 12 years in 59 % of the patients. Another study reported increase in meniscal extrusion from 2.7 mm at 6 months to 3.6 mm at 4.4 years follow-up [65].

Whether MAT is chondroprotective is still a subject of debate. Most studies on this topic have small cohorts and short follow-up and might not be able to detect the chondral changes of osteoar-thritis that happen over time. Chalmers et al. [18] reported no change in Kellgren-Lawrence (K-L) grading in 5 of 10 patients (50 %) at 3.3 years, while Ha et al. [29] reported no change in K-L grade in 78 % at 2.6 years and worsening in 22 %. Vunderlinckx et al. [88] reported no change in K-L grade in 58 % after a mean follow-up of 8.8 years.

The radiographic changes depend on the imaging modality, grading system and the follow-up time. Carter et al. [16] reported no change in 94 % of the patients at 2 years, while there were degenerative changes at 10 years. In a longterm follow-up study of 23 patients, six patients had grade 2 degenerative changes, and five patients had grade 3 degenerative changes at 14 years. All patients with degenerative changes had received lyophilized grafts, and the mean Lysholm score was 75 at 14 years [89].

Good healing rates are reported based on MRI and second-look arthroscopy. Van Arkel et al. reported higher healing rates evaluated by arthroscopy than MRI, suggesting that MRI may underestimate healing of the meniscal allograft [79]. Some studies reported up to 100 % healing evaluated on MRI [10, 47, 52]. Ha et al. reported a 72 % healing and 28 % partial healing, while van Arkel reported complete healing in 63 %, partial healing in 26 % and no healing in 11 %. On second-look arthroscopy, the patients evaluated as partially healed on MRI were healed, and those evaluated as no healing were partially healed.

17.7.4 Return to Sports

Few studies address the issue of return to sports after MAT. There is still no consensus as to when players can return to preinjury activities. There is also a debate whether a patient should return to sport at all after MAT. Alentorn-Geli et al. reported an 85.7 % return to sports after 15 MATs on soccer players [5]. Chalmers et al. [18] have also reported high rates of return to sports, with a 77 % rate of return to preinjury level of performance in 13 high-level athletes. As with several other MAT studies, the limitation is the sample size and the retrospective nature of the studies.

17.7.5 Complications

The complication rates vary a lot in the literature depending on the authors' definition of failure. Rosso et al. reported a weighted average complication rate of 10.6 % in their systematic review, with tear of the graft being the most common (60 %) of all complications. Higher failure rates are reported in the cryopreserved meniscus allografts than the fresh-frozen grafts. Some authors have argued that the fixation type on the medial side, soft tissue versus bone block, could affect the observed results. Bone block fixation theoretically provides better fixation, improved healing potential and a reduced risk for extrusion. This is important in restoring the joint biomechanics and loading. However, Rodeo reported higher histological scores in suture only MATs compared to bone plugs. Clinical studies have not reported any difference in patient-reported outcomes between the two fixation methods. However, suture technique was associated with higher failure rates including meniscus extrusion and high complication rates [1].

Conclusion

In summary, the studies reporting results after MAT are mostly level 3 and 4 studies (case series). Clinical results are good in the short and midterm. Radiological studies show a high percentage of meniscal extrusion on MRI, but this does not correlate with clinical outcome. Bony fixation is associated with less extrusion than soft tissue fixation. There is little joint space narrowing in the short and midterm, but significant after 10 years. Complication rates are around 10 %, with graft tear being the most common [45].

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