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Meniscal allograft transplantation

History

The surgical treatment of meniscal lesions is the most common procedure in the orthopaedic field today. Over 400,000 surgical cases involving the meniscus are being performed annually in Europe and over 1 million in the United States. The majority of these lesions result in a meniscectomy, while only a small percentage can be successfully repaired. The discovery 50 years ago that complete removal of a meniscus in the knee joint led to development of cartilage degeneration in the long term changed substantially the therapeutic approach to this common work or sports injury (1).

Total meniscectomy is now almost completely abandoned in favor of partial meniscectomy and meniscus-repairing procedures. Both procedures have the theoretical advantage of being less damaging to the articular cartilage. Long-term data to substantiate this hypothesis are, however, still missing. Nevertheless, total or subtotal meniscectomy remains necessary for large irreparable tears. In case of a meniscectomy, it appears logical to substitute the lost meniscal tissue in order to prevent cartilage degeneration, to relieve pain, and to improve function.

In order to restore normal knee biomechanics and anatomy and thus prevent further cartilage degeneration after meniscectomy, a number of surgical approaches including the use of autologous or allogenic tissues were being suggested, e.g., tendon, pediculated Hoffa fat pad, periosteal tissue, perichondral tissue, meniscal allografts, meniscal scaffolds based on native polymers (collagen and hyaluronic acid), or purely synthetic scaffolds such as poly-lactic acid, poly-glucuronic acid, and poly-urethane (2–8). Besides meniscal allografts, a collagen type I-based meniscal scaffold (CMI®, Regen Biologics, Franklin Lakes, NJ, USA), and a poly-urethane-based scaffold (Actifit®, Orteq, London, UK), none of these tissues have advanced to human clinical use.

While scaffolds are mainly used to substitute for partial loss, meniscal allografts are generally used in total or subtotal meniscectomized patients.

Meniscal allograft transplantation was first introduced into clinical practice by Milachowsky *et al.* in 1989. The senior authors started performing this type of procedure in the same year. We can now look back on a well-established series of over 250 patients treated with this type of surgery.

Biological basis

The general biological basis of allograft transplantation is the concept of a timely colonization of the acellular scaffold or allograft tissue by host cells, which are probably derived from the synovium and joint capsule (Fig. 1) (9,10). The phenotype of these host-derived scaffold-colonizing cells ultimately determines the biochemical composition and biomechanical behavior of these repopulated scaffolds or tissues.

Another critical variable in this approach is the time needed for colonization of the scaffold or tissue: since these scaffolds or tissues are biodegradable, the colonization and healing by host cells should be faster than the degradation process, for the regeneration or healing of the meniscal substitute to be successful.

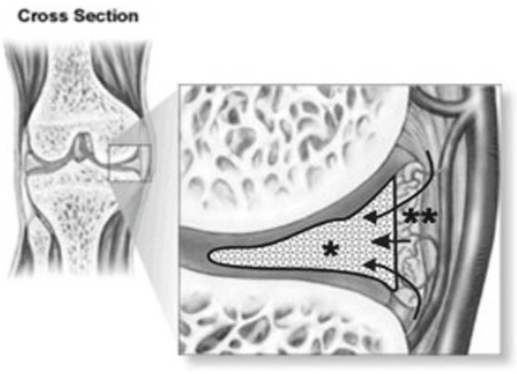

Fig. 1 – Acellular meniscal grafts or scaffolds (*) are colonized by host cells (arrows) which are probably derived from the synovium and the joint capsule (**).

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Previous animal studies have provided evidence that fresh "viable" and deep-frozen "acellular" meniscal allografts are quickly invaded by host cells within 1 month after transplantation (9,11). In the human model, however, only limited data are available. A previous study performed at our institution has provided evidence that this process of colonization is considerably slower in the human model: DNA fingerprint analysis, performed on human viable meniscal allograft biopsies taken up to 36 months after transplantation, showed that these allografts contained only donor-derived cells in a number of cases (12). These data substantiate observations published elsewhere on transplanted human deep-frozen meniscal allografts and collagen scaffolds. Histological sections of these specimens showed a decreased cellularity after transplantation, indicating decreased repopulation of the graft (10–13). Hence, an increase of the initial cell number at the defect site and thereby a decrease of the time needed for colonization can be accomplished by (1) transplantation of an in vitro cultured "viable" meniscal allograft, (2) seeding autologous cells with a proven meniscus repair potential on or in a biodegradable scaffold or allograft prior to implantation, or (3) structural and chemical modification of the scaffold or graft to enhance cellular ingrowth. Except for the transplantation of viable meniscus allograft, most of these proposed strategies are still under investigation.

In the clinical situation, several graft preservation techniques are available: lyophilization, deep-freezing, cryopreservation, and cultured or so-called "viable" allografts. Except for lyophilization, no significant clinical differences have been observed between the different preservation techniques (14,15). Lyophilization, on the other hand, has been abandoned due to inferior tissue quality and increased risk of clinical failure (16–19). Deep-freezing renders the graft completely acellular but preserves its biomechanical characteristics. Cryopreservation has been shown to preserve only 10–40% of the meniscus cells vital and functional (20,21). Preservation of meniscus cell viability and functionality can be guaranteed for 2–3 weeks if the meniscus allograft tissue is cultured in vitro using standard culture medium supplemented with 20% acceptor serum, the so-called "viable meniscus allograft" culture protocol (22). The authors have extensive experience with both deep-frozen and viable allografts (23). The biological activity of the cells within the "viable" scaffold remains to be determined and is subject of current clinical research protocols within our department.

Indications and contraindications (24)

Indications

The indications for meniscal allograft transplantation have yet to be comprehensively defined. Current recommendations suggest that the procedure is indicated in three clinical scenarios:

1. Young patients with a history of meniscectomy who have pain localized to the meniscus-deficient compartment, a stable knee joint, no malalignment, and articular cartilage with only minor evidence of osteochondral degenerative changes (no more than grade 3 according to the International Cartilage Repair Society (ICRS) classification system) are considered ideal candidates for this procedure. Because of the more rapid deterioration in the lateral compartment (25), a relatively common indication for meniscal transplantation would be a symptomatic, meniscal-deficient, lateral compartment.
2. ACL-deficient patients who have had prior medial meniscectomy (who might benefit from the increased stability afforded by a functional medial meniscus) in conjunction with concomitant ACL reconstruction. It is the author's conviction that an ACL graft is significantly protected by the meniscus allograft as much as the meniscus is protected by an ACL graft (26).
3. A third context for meniscal transplantation has also been advocated by some. In an effort to avert early joint degeneration, young, athletic patients who have had complete meniscectomy might be considered as meniscal transplantation candidates prior to symptom onset (27).

Contraindications

Advanced chondral degeneration is considered as a contraindication to meniscal allograft transplantation, although some series suggest that cartilage degeneration is not a significant risk factor for failure (23). In general, articular cartilage lesions greater than grade 3 according to the ICRS classification system should be of limited surface area and localized. Localized chondral defects may be treated concomitantly — the meniscus transplantation and the cartilage repair or restoration may benefit each other in terms of healing and outcome (28). Chondrocyte transplantation or osteochondral grafting procedures should be performed after completion of the meniscal transplantation in order to prevent accidental damage to the patch or graft during meniscal allograft insertion (29). Radiographic evidence of significant osteophyte formation

or femoral condyle flattening is associated with inferior postoperative results as these structural modifications alter the morphology of the femoral condyle (20). Generally, patients over age 50 have excessive cartilage disease and are suboptimal candidates.

Axial malalignment tends to exert abnormal pressure on the allograft leading to loosening, degeneration, and failure of the graft (15). A corrective osteotomy should be considered for greater than 2° of deviation toward the involved compartment, as compared with the contralateral limb mechanical axis. Varus or valgus deformity may be managed with either staged or concomitant high tibial or distal femoral osteotomy (20). However, as in any situation in which procedures are thus combined, it becomes unclear which aspect of the procedure is implicated in symptom resolution, such as relief of pain (15).

Other contraindications to meniscal transplantation include obesity, skeletal immaturity, instability of the knee joint (which may be addressed in conjunction with transplantation as above), synovial disease, inflammatory arthritis, and previous joint infection.

Technique

Preoperative considerations

In contrast to the use of deep-frozen allografts, a strict time schedule from harvest to transplantation is mandatory for viable allografts. The transplantation of viable meniscal allografts implies the availability of viable donor tissues, cultured in vitro immediately following harvest. Sizing of the graft is critical for correct implantation. For deep-frozen allografts, the mediolateral and anteroposterior lengths of the tibial plateau of the receptor are measured on a calibrated x-ray and transferred to the tissue bank. Since viable meniscal allografting is more limited in size options due to the fact that there is only one donor and a limited number of acceptors, the most appropriate acceptor is chosen based on corresponding donor-acceptor height and weight criteria. Once a patient is deemed to be a candidate for this type of procedure, 30–50 ml of autologous serum is prepared and frozen at −21°C. The waiting time for a viable meniscal allograft averages 2 months – ranging from 14 days to 6 months – at our institution. Once an appropriately sized meniscal allograft is harvested, the patient is notified and an operation is planned within the next 14 days.

Surgical technique

Introduction

The purpose of this technical chapter is to present medial and lateral meniscal allograft transplantation (1) as an open procedure or (2) as an arthroscopically assisted procedure. Both techniques use primarily soft tissue fixation of the allograft to the native meniscal rim. Additional transosseous fixation of the anterior and posterior horn is used in the arthroscopic technique, while a tag on the anterior horn is used in the open procedure for soft tissue-bone fixation.

Anesthesia and surgical preparation

These items are identical for the open and arthroscopic procedure. The choice of anaesthesia is made in consultation between the surgeon, the anaesthesiologist, and the patient and depends on the patient's age, comorbidity, and history with regard to previous anesthesia. General anesthesia is preferred at our institution.

The patient is then positioned supine on the operating table. A lateral leg-holder is positioned at the height of the tourniquet with the leg positioned in 90° of flexion. A foot holder is used to hold the leg in 90° and 110° of flexion as needed. Previous skin incisions are marked. The limb is exsanguinated and the tourniquet is inflated. The limb is then prepared with chlorhexidine gluconate-alcohol solution (Hibitane, Regent Medical Overseas Limited, Manchester, UK) and draped at the mid-thigh level.

Allograft preparation for the open procedure

As previously described elsewhere, the allograft is positioned and fixed on a specially designed cork board with three 25-gauge needles (Fig. 2A) (30). With a scalpel, the residual synovial tissue is dissected from the allograft meniscus at the meniscosynovial junction level and discarded.

The upper side of the allograft is marked with a methylene blue skin marker.

Horizontal 2/0 polydioxanone surgical sutures (PDS II mounted on a double small needle, Ethicon, Somerville, NJ, USA) or 2/0 non-absorbable polypropylene sutures (Prolene mounted on a double small needle, Ethicon, Somerville, NJ, USA) are placed every 3–5 mm through the posterior horn, the body, and the anterior horn of the allograft and fixed onto a specially designed suture holder (holder A) (Fig. 2A). The senior surgeon (RV) prefers the use of 2/0 Prolene sutures for the posterior horn since this suture material comes with slightly smaller needles and therefore has easier surgical handling in the more narrow posterior joint space. The sutures are fixed onto the suture

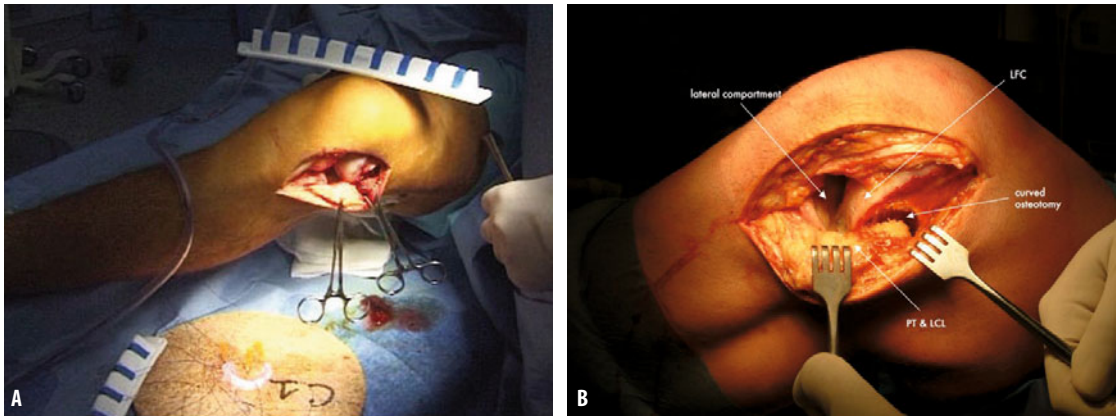


Fig. 2 – (A) Open meniscal allograft transplantation. A lateral parapatellar incision is made, with the knee in 90° of flexion, to gain access to the lateral compartment of the joint. (B) Open meniscal allograft transplantation. To further open the lateral compartment, the LCL and PT are detached with a curved osteotomy on the femoral side.

holder in sequence from posteriorly to anteriorly. Generally, six to eight sutures are needed to cover the complete allograft.

Open meniscal allograft transplantation

A medial or lateral parapatellar incision of approximately 8 cm is made with the knee in 90° of flexion to gain access to the involved compartment of the knee joint (Fig. 2A). The joint capsule is then opened and the anterior horn of the meniscus remnant is transected.

For the lateral procedure, the iliotibial band is released subperiostally from its distal attachment. To further open up the lateral compartment, the insertions of the lateral collateral ligament (LCL) and popliteus tendon (PT) are detached with a curved osteotomy on the femoral side (Fig. 2B) The center of the osteotomy bone block is first predrilled with a 2.7-mm drill. This facilitates subsequent refixation with a screw and washer. The osteotomy is done in a clockwise direction from the 8 o'clock position to the 4 o'clock position and is approximately 1.5 cm deep and conically shaped. The bone block is gently folded out using a bone clamp, and then the osteotomy is completed inferiorly from the 4 o'clock to the 8 o'clock position using the osteotome. The lateral joint space can now be opened up easily 1–2 cm by placing the knee in the figure of 4 position in 70–90° of flexion with the index foot positioned across the contralateral limb (Fig. 2A).

For the medial procedure, the medial collateral ligament is detached on the femoral side with an osteotomy (31). A flake osteotomy (0.5–1 cm in thickness) is done with a straight osteotome at the level of the medial femoral epicondyle. The soft tissues posterior to the medial collateral ligament are left in continuity. By gently placing the knee in a valgus position, the medial compartment can now be opened up in a controlled fashion.

The meniscus remnant is trimmed preferably to a stable meniscal rim with a scalpel anteriorly and with arthroscopic instruments posteriorly. Most often, the insertion of the posterior horn is still intact and in continuity with the tibial plateau. The insertion of the posterior horn is also trimmed to fit the allograft. The meniscal rim deserves surgical attention, as it serves as a strong envelope encapsulating the medial or lateral compartment of the knee.

The meniscal remnant level is then marked with a small mosquito clamp anteriorly as landmark for the correct level of subsequent fixation of the allograft. Next, the previously prepared viable meniscal allograft is introduced into the knee compartment. The sutures are taken from the holder in the correct sequence from posteriorly to anteriorly and driven through the meniscal rim one by one in an all-inside fashion from inferiorly to superiorly and transferred to a second suture holder (holder B), again in a sequence from posteriorly to anteriorly. The lateral allograft is also sutured to the popliteus tendon. We have found on follow-up arthroscopies that the popliteal hiatus will recreate itself naturally. The insertion of the anterior horn of the meniscus is not yet sutured at this stage of the operation. Once the sequence of suture transfer from holder A through the meniscal rim (and popliteal tendon) to holder B is completed, the allograft is introduced into the compartment by gently pulling on each suture in a sequence from posteriorly to anteriorly. Generally, this procedure has to be performed progressively to establish a secure fit of the allograft to the meniscal rim. The suture knots are then securely tied and cut. A fine-tipped suture driver and knot pusher are frequently

required to securely tighten the posterior sutures. The knee is now positioned again in a normal 90° flexed position. The bone block of the collateral ligament and popliteus tendon is repositioned and fixed using a 35- or 40-mm 2.9 AO cancellous screw with a spiked washer. The anterior horn of the allograft is then fixed to the tibia using an anchor (GII, Depuy Mitek, Raynham, Massachusetts, USA). The Hoffa fat pad and knee capsule are closed using interrupted Vicryl 1/0 (Ethicon, Somerville, NJ, USA) cross-stitches after haemostasis.

Allograft preparation for the arthroscopic procedure

The allograft is positioned and fixed on a specially designed cork board with three 25-gauge needles. With a scalpel, the residual synovial tissue is dissected from the allograft meniscus at the meniscosynovial junction level and discarded.

The upper side of the allograft is marked with a methylene blue skin marker.

Non-resorbable high-strength (Fiberwire, Arthrex, Naples, USA) sutures are placed in the anterior and posterior horn of the allograft. Generally, three whipstitches are placed on the inner and outer rim of the horn of the allograft (Fig. 3). An additional vertical non-resorbable suture (Ethibond 2, Somerville, NJ, USA) is placed at the posteromedial or posterolateral corner of the medial or lateral allograft, respectively. For the lateral allograft, the posterolateral suture is positioned just anteriorly to the popliteus tendon hiatus as this will serve as a landmark during arthroscopy (Fig. 3).

Arthroscopically assisted lateral meniscal allograft transplantation

The classic anteromedial and anterolateral portals are made. An additional anteromedial portal is positioned very medially to gain easy instrumental access for the debridement and resection of the anterior portion of the native lateral meniscus. Using shaver and punch, the remnant meniscus is debrided to the level of the meniscal rim.

A modified ACL aiming device, with a low-profile tip, is inserted through the medial portal and positioned at the anatomical posterior horn of the lateral meniscus just posterior to the ACL (Fig. 4). A guide pin is drilled first and subsequently overdrilled by a 4.5-mm cannulated drill. A double-looped metal wire is introduced through the tunnel from outside-in and picked up intra-articularly with an arthroscopic grasper and pulled out through the lateral portal. Subsequently, a suture passer (Acupass, Smith and Nephew, Memphis, Tennessee, USA) is introduced twice from outside-in just anterior to the LCL and the popliteus tendon into the joint: one just below and the second above the native meniscal rim (Fig. 5). The looped wires are picked up and pulled out again through the lateral portal. Next, the posterior horn pull suture and the posterolateral pull suture are pulled through using the double-looped metal wire and the double-looped suture pass wire. The prepared lateral allograft is subsequently introduced into the lateral

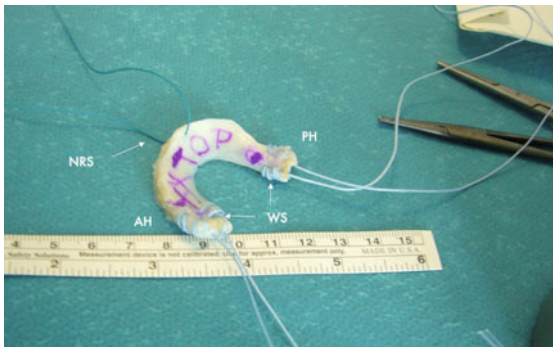


Fig. 3 – Prepared lateral meniscal allograft for arthroscopic meniscal transplantation. Whip stiches (WS) on the inner and outer rim of anterior (AH) and posterior horn (PH). A vertical non-resorbable suture (NRS) is placed on the posterolateral corner, just anterior of the PT hiatus.

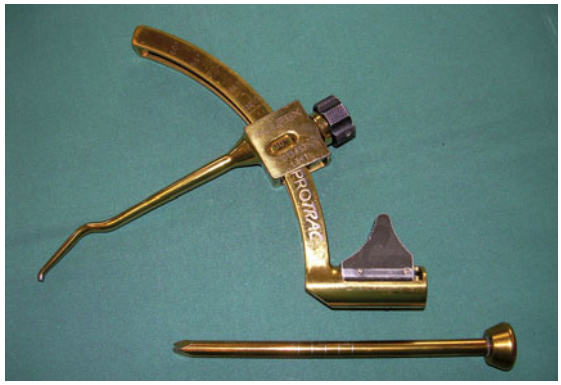


Fig. 4 – Modified ACL aiming device, with low profile tip. This device is positioned at the anatomical posterior horn of the lateral meniscus, just posterior to the ACL.

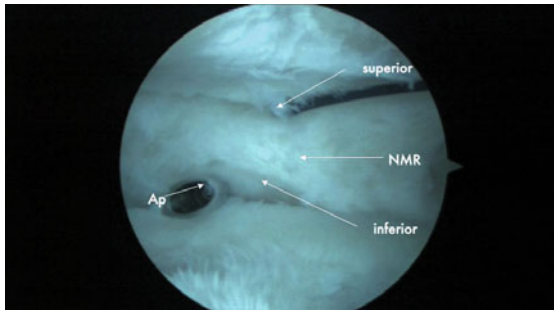


Fig. 5 – A suture passer (Acupass® Ap) is introduced twice from outside-in, just anterior to the LCL and the PT, superior and inferior of the native meniscal rim (NMR).

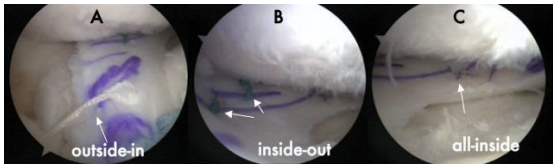


Fig. 6 – Arthroscopic views of a lateral meniscal allograft in place. (A) Anterior horn, outside in vertical. (B) Corpus, inside out oblique. (C) Posterior horn, all- inside Fastfix®.

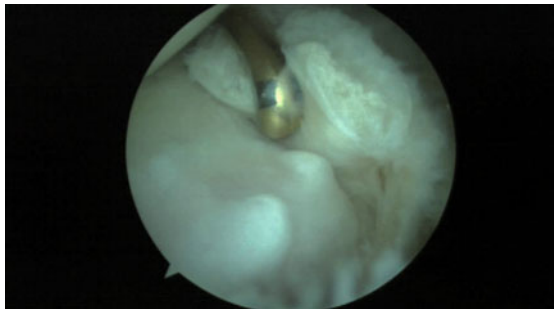


Fig. 7 – Arthroscopic view of the posteromedial portal used in arthroscopically assisted medial meniscal allograft transplantation. The custom ACL guide in introduced through the intercondylar notch on the anatomical posterior horn insertion of the native medial meniscus.

compartment throughout an enlarged lateral portal by pulling progressively on the posterolateral pull suture and the posterior horn pull suture. Care should be taken that the graft does not flip upon introduction and that pull wires do not intertwine. Risk for intertwining wires is greatly reduced by using a double-looped metal wire for the posterior horn (Fig. 6).

The posterior horn is now positioned correctly. Its position can be slightly modified more toward the posterolateral corner or more toward the posterior horn by pulling more on the posterolateral or posterior horn traction wire. One or two all-inside meniscal fixation devices (Fastfix, Smith and Nephew, Memphis, Tennessee, USA) are used to fix the allograft to the meniscal rim. Fixation should be started in the posterolateral corner. Subsequently, inside-out horizontal Ethibond 2/0 sutures are used for fixing the body of the allograft. The anterior horn is fixed using outside-in PDS or Ethibond 2/0 sutures.

Prior to making the sutures knots, the anterior horn is introduced into the knee joint and the anatomical insertion site is identified and prepared is a same manner as for the posterior tunnel. If necessary, its position can be slightly adapted to the graft position. Similar to the procedure of the posterior horn, the anterior tunnel is prepared and the traction suture is pulled through.

First, the meniscal inside-out sutures are knotted. Subsequently, the anterior and posterior horn traction sutures are knotted to each other over a bone bridge on the anteromedial side of the tibia. This procedure reduces the possibly stretched capsule and native meniscal rim tied to the meniscal allograft, by pulling on the anterior and posterior horn by a transosseous suture fixation.

Arthroscopically assisted medial meniscal allograft transplantation

A similar procedure as for the lateral allograft transplantation is performed for the medial allograft transplantation. However, some steps are different and will be highlighted in this section.

Additional to the classic anteromedial and anterolateral portal, a posteromedial portal should be used to identify the original posterior horn attachments of the native meniscus (Fig. 7). Using the same drill guide, the transosseous tunnels can be prepared. These tunnels should be prepared starting on the anterolateral side of the tibia. This direction is more in line with the forces on the traction sutures.

A posteromedial traction suture is used, as in accordance to the lateral allograft. On the medial side, however, we lack a clear anatomical landmark such as the popliteal hiatus on the lateral side.

The anterior horn of the native medial meniscus may in some cases be very anterior on the tibial plateau resulting in a very short transosseous anterior tunnel.

Special note on soft tissue vs. bone block fixation (32–36)

Biomechanical cadaver studies have shown the superiority of a bony fixation over a soft tissue fixation technique, although a recent cadaver study showed comparable results. Bony fixation however, has also been shown to be associated with increased risk for cartilage lesions if implanted incorrectly and an increased immunological potential due to the presence of allogeneic bone. It is the authors' experience that perfect allograft size matching is essential if bony fixation is to be used. A malpositioned bone block or plug can inflict damages to the overlying cartilage. Too small a graft will result in a need to overtension the inside-out sutures and possible failure of the soft tissue fixation. Therefore, limited oversizing of the graft is commonly advocated using bone plugs or blocks. Separate bone plugs have the potential advantage that the implantation can be somewhat more variable compared to a single bone block. In addition, on the lateral side, a straight bone block sometimes induces the need to sacrifice some posterolateral fibers of the ACL.

Today, clinical and/or radiological differences have not been shown between soft tissue or bone block fixation.

Rehabilitation

Rehabilitation is initially focused on providing mobility to the joint without endangering ingrowth and healing of the graft. Therefore, 3 weeks of non-weight-bearing are prescribed followed by 3 weeks of partial weight-bearing (50% of body weight). Progression to full weight-bearing is allowed from week 6 on to week 10 postoperatively. The use of a knee brace is not strictly necessary and depends on the morphology and profile of the patient. For the same reasons, the range of motion is limited during the first 2 weeks from 0 to 30, to increase by 30° each 2 weeks.

Isometric muscle tonification and co-contraction exercises are prescribed from day 1 post-surgery on. Straight leg raise, however, is prohibited during the first 3 weeks. Proprioception training is started after week 3.

Swimming is allowed after week 6, biking after week 12, and running is progressively promoted starting at week 20.

Results

Clinical outcome

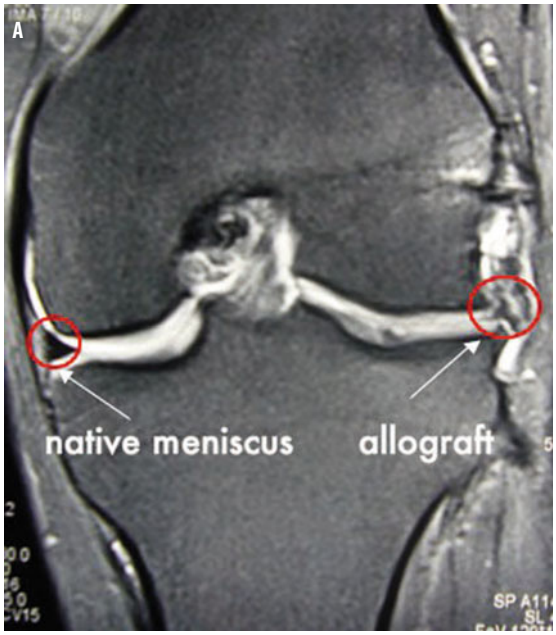
All mid- and long-term studies have shown that medial and lateral meniscal allograft transplantation significantly reduces pain and improves function of the involved knee joint (7,20,37–43). Despite significant improvement in the long run, substantial disability and symptoms have been observed at more than 10 years of follow-up as documented with patient-related outcome scoring systems (Knee Osteoarthritis Outcome Score) (23).

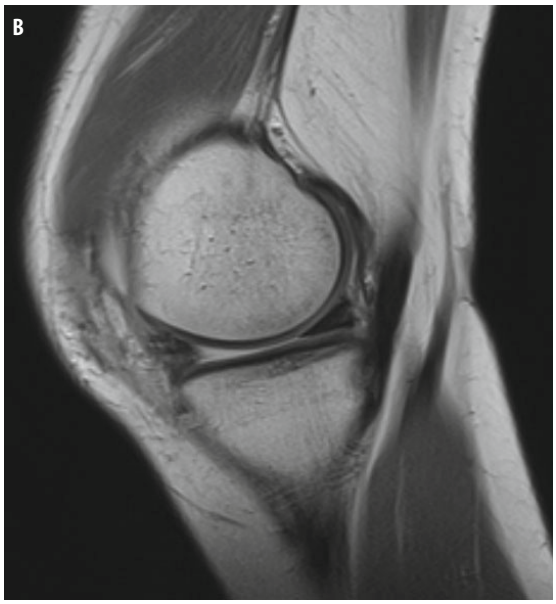
In a recent series, mean survival times and cumulative survival rates of approximately 70% at 10 years were comparable between isolated lateral and medial allografts (7). Previous studies have shown that risk factors for failure and reduced survival time are lower limb malalignment, ACL deficiency, and grade 4 cartilage lesions (37,39,44,45). Moreover, the additional beneficial effect of a corrective osteotomy in case of a varus malalignment and the importance of a stable knee joint have been clearly demonstrated (23). The exact position of an associated corrective osteotomy in the valgus knee needs further refinement. More recent studies have not confirmed a significant correlation between the initial cartilage status and clinical failure, challenging the contraindications for arthrosis severity (7,23).

Radiological outcome

In order to overcome the observed discrepancy between clinical outcome and the status of the meniscal allograft and to analyze any progression of degenerative articular changes after this type of surgery, objective outcome measures such as MRI have to be included in outcome studies (Fig. 7). Limited data are present in the literature reporting that meniscal allografting halts or slows down further degeneration (14,21). In one recent long-term study, progression of cartilage degeneration according to MRI and radiological criteria was halted in a number of patients, indicating a potential chondroprotective effect (23). A recent controlled large animal study was also able to confirm this chondroprotective effect (46). These data could support the use of prophylactic meniscal transplantation in meniscectomized patients without clinical symptoms, thus potentially limiting the cartilage degeneration secondary to a meniscectomy. Further prospective comparative studies are needed to test this hypothesis.

Using MRI, extrusion of the meniscal allograft has been described independent of the surgical fixation technique (Fig. 8). In our experience using soft tissue fixation in the open technique, the extrusion is observed in the corpus and anterior horn of the graft, while the posterior horn is most frequently within normal values (23,47). This extrusion lowers the functional surface of the graft and thus reduces its biomechanical function. The authors hypothesize that this extrusion is caused by both a biological as well as a biomechanical phenomenon. Attention has been mainly focused on the surgical fixation technique of the graft within the knee joint. Biomechanical cadaver studies have clearly shown the superiority of a bony fixation over a soft tissue fixation technique (48–50). Comparative clinical and radiological results, however, lack the power to substantiate this in vitro finding. Biological reasons for the observed extrusion post-transplantation could include progressive stretch and failure of the circumferential collagen bundle due to insufficient repair potential or increased catabolism. Future research should focus on the biology involved in ongoing metabolic and cellular processes after transplantation.





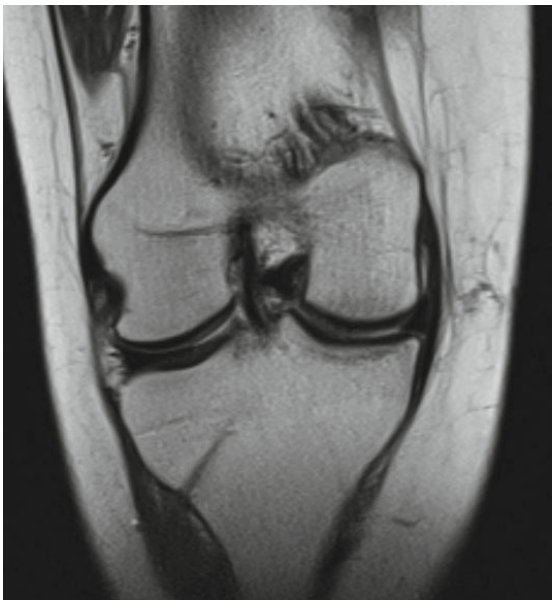


Fig. 8 – (A) MRI-image: extrusion of a lateral meniscal allograft and native medial meniscus in a left knee. (B) MRI-image: well-positioned medial meniscal allograft and native lateral meniscus in a right knee.

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