Meniscal transplantation: state of the art

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ABSTRACT
Meniscal resection is the most common surgical procedure in orthopaedics. When a large meniscal loss becomes clinically relevant, meniscal allograft transplantation (MAT) is a feasible option. However, although this technique has evolved since the ‘80s, there are still several controversial issues related to MAT. Most importantly, its chondroprotective effect is still not completely proven. Its relatively high complication and reoperation rate is another reason for this procedure not yet being universally accepted. Despite its controversial chondroprotective effect, nevertheless, MAT has become a successful treatment for pain localised in a previously meniscectomised knee, in terms of pain relief and knee function. We conducted a careful review of the literature, highlighting the most relevant studies in various aspects of this procedure. Precise indications, how it behaves biomechanically, surgical techniques, return to sport and future perspectives are among the most relevant topics that have been included in this state-of-the-art review.

INTRODUCTION
Meniscal injuries are one of the most common knee injuries. Their treatment is the most common surgical procedure performed by orthopaedic surgeons. The management of meniscal ruptures is currently evolving and most orthopaedic surgeons try to preserve the meniscus whenever possible. The natural history of a meniscus-deficient knee has been shown to involve poor outcomes over time due to higher peak stresses on the articular cartilage as a result of the decreased contact area. Unfortunately, large meniscal resections are sometimes inevitable. Meniscal allograft transplantation (MAT) is a potential solution to restore knee biomechanics, improve clinical outcomes and, possibly, delay the onset of knee osteoarthritis (OA).

This state-of-the-art article aims to provide an overview of the most accepted and the most controversial topics on MAT, starting from a historical perspective and ending in future trends and challenges.

Once upon a time. Historical perspective
Based on the knowledge that loss of meniscus tissue results in increased stress and subsequent degenerative wear of articular cartilage, Dieter Kohn in Hannover, Germany, started clinical trials using fat pad and quadriceps tendon autograft to substitute meniscus tissue.1 Milachowski from Munich, Germany, performed the first meniscus allograft transplantation in 1984 using lyophilisation as preservation method.4 Despite the observed shrinkage of the grafts, this study provided proof of principle that meniscus transplantation results in a remarkable clinical benefit.

A number of other European centres began work on meniscal transplantation at this time. In Belgium, Rene Verdonk pioneered viable meniscal transplantation, performing his first human meniscus allograft transplant in 1989.5 Believing that intact cellular function could provide an advantage over acellular frozen allografts, he developed and validated the technique for viable graft conservation in the laboratory. In 1991, Herman de Boer, from Heerlen in the Netherlands, reported a case of a lateral meniscus allograft transplant in a 48-year-old using a cryopreserved meniscus.6 de Boer, working together with Ewoud van Arkel, would go on to report clinical and radiological outcomes and survival after MAT.7 8

The first published report of free meniscal transplantation in North America came from John Garret in Atlanta.9 All the six patients included in his study showed minimal or no pain, and second-look arthroscopy in four cases revealed healing of the periphery and horns. In 1997, John Cameron from Toronto reported what was then the largest series of meniscal allograft transplants, with 67 procedures performed between 1988 and 1994 using fresh-frozen, gamma-irradiated tissue.10 This work built on the experience of Allan Gross, who pioneered the use of osteochondral allografts and used a number of composite osteochondral and meniscal allografts.11 Frank Noyes, from Cincinnati, has been a leading proponent of meniscal allograft preservation,12 in vivo motion13 and extrusion.

Kevin Stone, from San Francisco, along with Steve Arnoczky, Bill Garrett and Marlowe Goble, from Utah, began the Meniscal Transplantation Study Group in 1986. In addition to his research output, encompassing work on meniscal allograft sizing and survival, as well as meniscal replacement,14–17 Stone has chaired the annual meeting of the Meniscal Transplantation Study Group since the mid-1990s. In Chicago, Brian Cole has been an active researcher in the field. His contribution has been wide ranging, from basic science to clinical studies, including a number of prospective outcome studies of MAT in conjunction with articular cartilage repair procedures, chondral repair plus osteotomy and femoral osteochondral allografting.18 In Asia, Seong-Il Bin and Jong-Min Kim’s team, from South Korea, have published a large number of studies regarding meniscal transplantation. Much of their work has focused on radiological outcomes and the correlation between meniscal extrusion and clinical outcome.19 20

In Australia, Gregory Keen and Peter Myers have been major proponents of meniscal transplantation, reporting three decades ago a meniscal transplantation in a professional footballer21 or recently publishing a systematic review of the technical...
of joint conformity therefore results in increased loading in the central area of the compartment, if it were not for the critical role of the lateral meniscus in distributing approximately 70% of the load.24

Secondary functions include providing stability to the joint by means of the peripheral anchor points of the meniscus to the tibial plateau. This is particularly important for the medial meniscus—due to its postero-medial meniscotibial insertion, which aids in providing anterior translational stability—and also for the lateral meniscus, which helps to provide anterolateral rotatory stability. Furthermore, the menisci can aid in the lubrication of the joint by spreading and applying synovial fluid to the articulating surfaces.24

Loss of the functional status of the menisci can therefore reduce the ability of the menisci to perform the aforementioned functions. Functional loss is determined when the circumferential fibre orientation is disrupted, thereby limiting the meniscus to distribute load. A radial tear-out to the periphery, or a posterior root transection is therefore similar in function to a subtotal meniscectomy.23 This is particularly important in the lateral compartment, as the lack of joint conformity and subsequent load distribution has been shown to result in excessive compressive and shear forces on the articular surface with resultant rapid degenerative change.

The biomechanical goal of meniscal transplantation is therefore to re-establish the functional status of the meniscus, providing protection to the joint surface and, as such, symptom relief. Cadaveric studies have demonstrated that size-matched donor grafts can closely recapitulate the normal contact mechanics of the joint under load.25 While a number of studies have shown an improvement in contact pressures with bony fixation of grafts over soft tissue fixation alone,26 this has not resulted in improved clinical outcomes in short-term or long-term follow-up.27

Lastly, one of the other indications for MAT is to aid in providing stability as a concomitant procedure to anterior cruciate ligament (ACL) reconstruction. Many clinical studies have demonstrated the importance of the menisci in achieving good outcomes following ACL reconstruction,28 with a number of biomechanical studies demonstrating the important role the menisci have to play to help control anteroposterior (AP) and rotatory stability.29 The addition of a MAT, particularly a medial graft, to a revision ACL reconstruction in a patient who lacks the posterior buttress of the meniscus, may help to improve outcome. Furthermore, the meniscus may also reduce the postero-rivial slope of the knee,30 which is correlated with ACL reconstruction failure.31

How does MAT work? Biomechanics

The native menisci are two wedge-shaped fibrocartilaginous tissues situated between the femur and tibia. Their specialised anatomy and structural composition provide a number of key biomechanical roles within the knee joint.

Both menisci have very strong insertional ligaments anteriorly and posteriorly, with type I collagen fibres running circumferentially within their substance.28 Radial tie fibres of collagen hold the bundles of circumferential fibres together, so that on axial loading, the compressive forces produce hoop stresses that are able to withstand load. In the surrounding extracellular matrix, the high concentration of negatively charged glycosaminoglycans provides a hydrophilic environment, which accounts for the high water content (60%–70%), also aiding in resisting compressive deformation.

The medial meniscus is more c-shaped, covering approximately 60% of the surface area of the plateau, with the lateral meniscus covering approximately 80%. This is extremely important due to the relative topographical anatomy of each compartment. The medial compartment comprises a convex femoral surface articulating with a concave tibial surface. The medial menisci therefore contribute to approximately 50% of the load. Conversely, the lateral compartment comprises a convex femoral surface on a relatively flat if not convex tibial plateau. The resulting lack

aspects of the procedure.22 In conclusion, the current practice of MAT has evolved over the last century, from the early work of Fairbanks, who understood the importance of meniscus preservation, to the early pioneers of the procedure in Europe and North America.

State of the Art

Key articles


When and when not? Indications and limits

Meniscus allograft transplantation (MAT) is a potential biological solution for the symptomatic, meniscus-deficient patient who has not yet developed advanced OA. However, MAT is an integral part of a surgical algorithm to treat a symptomatic knee after loss of meniscus function.22 This algorithmic approach to the postmeniscectomy knee includes, in the first place, an evaluation of overall lower limb alignment. Malalignment—when present—should be corrected by osteotomy. A corrective osteotomy is considered the golden standard treatment for a malaligned knee with significant meniscus loss. In other words, a lateral meniscus transplantation should not be performed in a valgus-aligned lower limb. Moreover, a corrective osteotomy is generally clinically sufficient for the treatment of the postmeniscectomy knee and may not necessitate the combination with MAT. Second, ligamentous instability and more specifically
Figure 1  Coronal MRI of a left knee showing absence of the lateral menisci (arrow) in the lateral femorotibial compartment, with preserved articular cartilage.

Figure 2  Coronal MRI of a right knee. Note the absence of the lateral menisci in the lateral femorotibial compartment, with advanced kissing osteochondral degeneration (arrows).

ACL tears should be addressed surgically prior to or in combination with MAT. Ligament reconstruction will protect MAT, as much as MAT will protect the ACL reconstruction. Third, the 2015 Consensus Statement on the Practice of Meniscal Allograft Transplantation recommends MAT for three groups of patients:33 34

1. The first scenario is young patients who have undergone a meniscectomy but continue to have pain in the meniscus-deficient compartment. The knee joint should be stable and with normal alignment, and osteochondral degenerative changes in the articular cartilage should be no higher than grade 3 of the International Cartilage Repair Society (ICRS) classification system (figure 1). As the lateral compartment undergoes degeneration more rapidly, meniscal transplantation is commonly indicated for this side of the knee if the injury is symptomatic and meniscal deficient.

2. The second group refers to ACL-deficient patients who had undergone a previous medial meniscectomy while having an ACL reconstruction concomitantly. A functional medial meniscus in these patients may increase stability.33 It is the authors’ conviction that an ACL graft is significantly protected by the meniscus allografts as much as the meniscus is protected by an ACL graft.

3. Young, athletic patients who have had complete meniscectomy (and who might be considered meniscal transplantation candidates prior to symptom onset in an effort to avert early joint degeneration). This third context for meniscal transplantation has also been advocated by some but is still debated within International Meniscus Reconstruction Experts Forum (IMREF).

Fourth, it has been shown that the presence of cartilage degeneration is a prognosticator for MAT failure.35 36 Thus, the presence of cartilage wear in the affected compartment significantly reduces survival of the knee joint. Surgical cartilage restoration is advised in these cases. While some authors consider advanced cartilage degeneration contraindicates MAT, such degeneration has not shown to be a significant risk factor in a number of US series.37 To be considered for meniscal transplantation, any articular cartilage lesion grades 3 and 4 of the ICRS classification system should be localised and limited in size. It may be advantageous in terms of healing and outcome to treat localised chondral defects during the MAT procedure concomitantly.38 Radiographic evidence of significant osteophyte formation or femoral condyle flattening (figure 2) is associated with inferior postoperative results as these structural modifications alter the morphology of the femoral condyle.39 Generally, patients over age 50 have excessive cartilage disease and are suboptimal candidates. Meniscal transplantation has other contraindications, such as obesity, skeletal immaturity, non-addressed knee instability, synovial disease, previous infection in the affected knee and inflammatory arthritis.33 34
How big? Graft sizing

One of the most important preoperative evaluations is sizing of the receptor knee compartment and identifying a matching meniscus allograft. A number of measurement techniques for the recipient compartment have been studied based on plain X-ray, CT, MRI and anthropometric data.

Clearly, if a graft is too big, its extruded position within the knee joint will be biomechanically suboptimal, resulting in a continued overload situation of the articular cartilage. In contrast, a too small graft will be exposed to an increased biomechanical load, which could result in early graft failure. Although few studies have focused on the consequences of size mismatching, a 5%-10% size difference appears to be well tolerated.40 41 Nevertheless, it is advisable to oversize rather than to undersize, since oversizing can be partially addressed and tuned surgically.

An aspect that remains currently underexposed in meniscus allograft transplantation is the specific anatomy of the anterior medial horn of both the allograft and the recipient compartment. Three types of medial anterior horn anatomy have so far been identified in anatomical dissection and MRI studies: the most common type 1 with an insertion posterior to the anterior tibial edge and lateral to the spine, type 2 with an insertion medial to the spine, and the least common type 3 with an insertion anterior to the anterior edge of the tibial plateau.42 We hypothesise that implanting a meniscus allograft posterior to the tibial edge (type 1 or 2) in a knee with former type 3 meniscus might result in overstuffedness of the anterior compartment, extension loss and increased stress in the graft.

Recipient compartment sizing is of utmost importance to subsequently order a matching allograft. No method to date, however, has been identified as the most reliable or the most user-friendly. The Pollard method is most commonly used and relies on calibrated AP and lateral radiographs.41 Nevertheless, it incorporates a number of flaws, mainly affecting lateral allograft sizing. The surgeon should be aware of the significant interindividual variability between the medial and the lateral compartment dimensions, mainly in the AP direction, as measured on plain X-rays. Yoon et al have introduced a modification based on a mathematical model that should increase accuracy.44 45 CT-based imaging is considered to be more precise but increases cost and exposes the patient to higher radiation.46 MRI of the ipsilateral or contralateral knee has been shown to be precise and accurate but is associated with increased cost. On the mid-coronal view, the distance from the meniscocapsular junction to the tibial spine is captured as the width of the allograft, while the AP dimension can be captured on the mid-sagittal image from the most anterior point to the most posterior point.47 48 Pre-existing extrusion of the capsule or remaining rim can potentially flaw these measurements. Regarding the anatomy of the native anterior horn of the medial meniscus, only a contralateral MRI can provide the necessary information. Anthropometric data using gender, weight and height of the patient and donor have been investigated and can provide reliable information.49

In addition to sizing of the recipient compartment and matching a corresponding allograft, it should be noted that the surgical technique, that is, bone block fixation versus soft tissue fixation using transosseous bone tunnels, has an impact on the sizing requirement. Bone block fixation implies perfect anatomical reconstruction of the anterior and posterior horns and thus relies strictly on finding the ideally sized allograft. Very little difference can be accepted between the measured recipient compartment and the matched allograft as this would result in a non-anatomical extruded (too big) or intra-articular (too small) position of the graft, or potential damage to the opposing articular cartilage by a bony prominence of the bone block. Thus, bone block fixation requires a well-functioning tissue bank with ample choice in graft size. The lower availability of grafts in Europe than in the USA has led to the development of the soft tissue with transosseous tunnels technique. This technique allows a more liberal sizing of grafts, preferably larger grafts. A larger graft can be implanted anatomically onto the anterior insertion site by pulling more grafts into the anterior transosseous tunnel, thus shortening the intra-articular portion of the graft (figure 3). A smaller graft can be positioned, in extremis, short of the anterior horn onto the tibial plateau (figure 4).

Keep it safe. Graft storage

The most appropriate technique to preserve menisci allografts in an acceptable condition until transplantation is still a matter of debate. The meniscus is mainly an avascular structure. Its

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**Figure 3** Arthroscopic view of a right medial meniscal transplantation. (A) There is a mismatch in this large allograft between the anterior horn (*) and the drilled anatomic anterior tibial tunnel. (B) The anterior horn of the allograft was partially introduced into the tibial tunnel to properly cover the desired surface.
mid-substance nutrition is fed by solute diffusion from the periphery on through the interfibrillar space. Subsequently, it seems logical to look for a storage technique that produces no change or minimal changes in the menisci’s collagen architecture.

► **Lyophilisation or freeze-drying.** This approach consists of freezing tissue under vacuum and freezing conditions and is an appropriate method to preserve viability of cells if cryoprotective solutions are used. This storage technique allows unlimited storage but it also alters the biomechanical properties and the size of the allografts. As a result, graft sizing during transplantation may be challenging. Freeze-drying is a process of preservation but not a means of sterilisation. As sterilisation of lyophilised tissues can be problematic, the process is often combined with irradiation at 25 kGy (2.5 Mrad). This strategy, however, may be detrimental to the tissue.

► **Freezing, deep-frozen or fresh-frozen.** This storage method is simple and has a very low immunogenicity. It had initially been proposed that this approach conserved the collagen net architecture intact despite damage to donor cells, but ultrastructural assessment from a later study showed that the freezing process caused serious collagen damage (figure 5).

► **Cryopreservation.** This process involves progressive cooling of the graft at 1°C/min in liquid nitrogen using a cryoprotective agent to minimise cellular damage. The graft is then maintained at −196°C. This process aims to protect viable donor cells through the use of a cryoprotectant that prevents intracellular ice crystals from forming, and has proven to be effective in cultured and isolated cells. Nevertheless, as cell survival in the tissue environment is reported to range from 4% to 54%, the proposed advantage of the method as a cell-preserving technique might be considered a secondary matter. From a biomechanical viewpoint, however, the approach does not seem to alter the meniscal ultrastructure. Compared with the deep-frozen method, cryopreservation is more demanding, difficult and costly. In conclusion, evidence to date suggests that keeping the normal collagen ultrastructure might be the cryopreservation’s main advantage as compared with the fresh-frozen procedure.

► **Fresh allograft or viable meniscal allografting.** This type of graft may be advantageous as it does not destroy cells and it keeps them viable by producing proteoglycans and collagen fibre structures. A normal or nearly normal cellular function can be expected from the moment of implantation. Although cellular repopulation occurs in the meniscal allograft after transplantation, donor cells survive for a long period of time, suggesting the superiority of a preserving system that is able to maintain cell viability. Procurement should take place as soon as possible and not longer than 12 hours after death. The graft can be safely kept for up to 15 days without a notable loss of cell viability. A recent study showed that this time period might be prolonged at least up to 4 weeks from harvesting if insulin-transferrin-selenium is used to maintain meniscal tissue instead of the host donor.

It is finally worth remembering that the use of fresh tissue in transplantation is always associated with a higher risk of disease transmission.

In conclusion, the two most commonly implanted menisci are either deep-frozen or cryopreserved, but fresh MATs have also grown in popularity (table 1). However, none of the conservation techniques have yet proven to be clinically superior to the others.

**ALLOGRAFT EXTRUSION**

The principal objective of meniscus allograft transplantation (MAT) is to alleviate symptoms generated in the involved compartment after meniscectomy. The aim of the surgeon is also to prevent or delay arthritic degeneration of the joint, but it has not yet been demonstrated whether this goal is systematically achieved. In the last decade, some troublesome issues related to this complex surgery have been recognised. Among them, the radial displacement or subluxation of the allograft (so-called extrusion) has been increasingly reported (figure 6) and is a cause of concern among surgeons. It seems that some degree of extrusion, less than 3 mm, is acceptable and considered normal. However, it is likely that the meniscal tissue cannot fulfil its function beyond this point as the hoop stresses are reduced. The resulting improper axial load transmission may lead to increased cartilage wear and finally to OA. However, the opposite can also
be true and the advanced cartilage wear may influence extrusion as has been seen in the natural history of the degenerative knee.63 Some other pathological conditions, like posterior root tears or complete radial tears, provoke failure of menisci biomechanics that can be diagnosed by their radial displacement outwards.64 Medial meniscus extrusion has also been reported in non-degenerative knees when the anterior root attachment site is located far anterior, in the intercondylar region of the tibial plateau, the so-called type I insertion.65

After MAT, extrusion seems to be a common phenomenon that appears shortly after surgery, although it does not tend to progress overtime.65 van Arkel et al66 published a series of MAT in which most grafts were seen in an abnormal position, either extruded or subextruded. Similarly, in Verdonk et al series,67 most of the meniscal allografts showed some degree of extrusion at a minimum follow-up of 10 years.

In the last decade, surgeons have been struggling to find out both the definitive cause and possible solutions for this extrusion. Some aspects of the surgical technique, such as the way the graft is implanted and fixed (namely, soft tissue vs bony fixation),68 the type of allograft (medial vs lateral)68 and the sizing method,69 have been looked at. In a prospective series of 88 MATs comparing soft tissue fixation versus bony fixation, Abat et al68 found a higher percentage of extruded meniscal tissue in the soft tissue fixation group. This suggested the superiority of bony fixation in terms of limiting extrusion. Koh et al68 evaluated a series of 73 lateral and 26 medial meniscus allografts by means of MRI at a mean follow-up of 32 months. Their results showed that lateral MAT extrudes significantly more than the medial MAT. Jang et al69 analysed 36 cases of MAT. Eighteen of them were preoperatively sized with the conventional Pollard method while they used a modified method in the rest, reducing the total size of the graft by 5%. In this latter group of MAT, the authors observed a decrease in the percentage of meniscal extrusion.

Several techniques have been proposed to limit or avoid meniscal allograft extrusion. Intended to address several factors related to extrusion, they are the anatomical implantation of the graft,70 the excision of peripheral osteophytes of the tibial plateau71 and the fixation of the meniscus allograft on the tibial surface.72 More recently, the reduction and fixation of the lateral capsule to the tibia has been put forth.73 Interestingly, based on the available evidence, extrusion seems to produce no adverse outcomes, either clinical or radiological. Therefore, it should be recognised that there is currently no real superiority of one surgical technique over another.33

How to do it. Surgical techniques

Preoperative planning

After complete physical assessment, an MRI of the involved knee is mandatory to confirm the loss of meniscal tissue as well as the status of the cartilage and any eventual associated condition. A routine radiographic examination should also be performed. It should include a long-standing AP view of both legs to measure lower limb alignment, a non-weight-bearing 30° flexion lateral radiograph and a 45° flexion weight-bearing posteroanterior view of both knees to assess joint line collapse.74

Patient positioning

The patient is placed supine in a conventional orthopaedic table either for medial or lateral MAT. A tourniquet may be used to keep the field clearer. It is mandatory to achieve a sufficiently large opening of the femorotibial joint line to permit work in the compartment. If the medial compartment is still tight, selective partial medial collateral ligament (MCL) release using the pie-crusting technique avoids iatrogenic injuries of the articulating surfaces without affecting knee stability.75 Conversely, the lateral compartment is approached putting the knee in a figure-of-four position, with the heel of the involved side over the contralateral limb.

Surgical technique

The currently reported techniques for MAT are mostly arthroscopically assisted. The meniscus allograft needs firm attachment at its insertion sites as well as good peripheral fixation. Fixation of the meniscal horns may be achieved either by suturing through bone tunnels or bony fixation. Peripheral

| Table 1 Pros and cons of each meniscal preservation technique |
|---------------|----------------|---------------|---------------|--------------|--------------|
| Type of graft | Preparation and logistic | Risk of disease transmission | Collagen net quality | Cost | Usage |
| Lyophilised | ++ | + | – | ++ | – |
| Fresh-frozen | + | + | + | + | +++ |
| Cryopreserved | ++ | + | ++ | ++ | ++ |
| Fresh | +++ | ++ | +++ | +++ | + |

Most relevant aspects of sizing the graft

► Oversizing is always preferable to undersizing.
► MRI, CT and X-ray have all been validated to match the meniscal allograft with the recipient compartment.
► Anthropometric data are the simplest method to calculate the required allograft.
► Bone-free MAT technique allows a larger size mismatching.

Figure 6  Coronal MRI of a left knee after medial and lateral meniscal transplantation. The medial meniscus is considerably extruded (white arrow) beyond the medial articular margin of the tibia (black arrow).
fixation is commonly done by combining standard suture techniques. Regularly, an all-inside technique is used at the posterior third of the allograft to avoid additional approaches. Either outside-in suture or inside-out suture techniques are preferred for the body and anterior horn zones. If tibial tunnels are to be used, they should be drilled at the menisci anatomical attachment sites with the help of a regular ACL guide or with a specifically designed aiming. The sutures are finally tied to each other on the anterior tibial cortex.

Bony fixation of the meniscal graft may be done using two plugs attached to their anterior and posterior horns or simply by means of a bone bridge linking them (figure 7). Most surgeons prefer bone plugs for the medial meniscus as the technique is less invasive and might preserve the tibial eminence. The more aggressive bone bridge procedure is reserved for the lateral MAT as it better preserves the native distance between horns. This technique requires the creation of a trough (bridge-in-slot technique) or, alternatively, a hemitunnel (keyhole technique) in the recipient tibial plateau where the bone graft is secured.

In summary, bony fixation techniques theoretically have greater biomechanical characteristics in terms of the restoration of the normal contact mechanics of the knee. The much simpler suture-only fixation has also reported good clinical outcomes although it exhibits a higher rate of allograft extrusion. Therefore, no study has shown a clear superiority of either techniques to date.

Regardless of the technique, what really matters is the anatomical restitution of the meniscus and its proper fixation because minimal misplacement of the tibial attachment sites may lead to improper functioning of the meniscal graft and inadequate fixation will end up in early allograft failure.

### Coming back. Rehabilitation and return to sports

Due to the lack of scientific data on postoperative management after MAT, most surgeons follow meniscal-suturing protocols. There are some controversies regarding weight-bearing. Some allow immediate unlimited knee loading, while others recommend from 2–3 weeks up to 6 weeks of non-weight-bearing.

Regarding range of motion (ROM), again, some authors advocate a period of immobilisation. However, as meniscal movement is minimal from 0° to 60°, it seems logical to recommend this ROM in the first 2–3 weeks after surgery. In the first weeks after surgery, therapy should consist of supervised continuous passive motion, paying particular attention to restoring full knee extension, decreasing swelling and pain control. Quadriceps strengthening with isometric exercises, passive and active motion, is also encouraged. After the first 3–4 weeks, therapy should involve flexion of the knee up to 90°, together with progressive weight-bearing, stationary biking and closed-chain kinetic exercises. At 6–8 weeks after surgery, the objective is full weight-bearing, and at 4–6 months straight line running is generally encouraged.

Consensus is lacking concerning forced flexion, pivoting movements and strenuous activities. However, avoiding these activities for the first 6–12 months may be considered reasonable based on the biology of meniscal healing and the available literature. Strenuous activity cannot be recommended, however, because repetitive high impacts can lead to producing unpredictable results in the allograft indemnity.

Recently, some authors have shown that MAT could also be performed in those patients willing to resume highly demanding and competitive sport activities (such as soccer, basketball, rugby and volleyball). They reported that 74% of patients were able to return to sport after a minimum rehabilitation period of 8 months. In half of the cases, patients returned to the same preinjury level. A similar return-to-preinjury level was reported in other series. However, their short follow-ups suggest conclusions be taken with caution. Research is still required into understanding how load influences graft survival and its fixation sites. Until these data are available, athletic activity should be limited to light sports. It is imperative that the patient be made aware of such limitations before the transplantation.

### Does it work? Clinical and radiological outcomes

MAT is not new, with the first cases being reported in the mid-1980s. With more and more case series being published detailing the results of MAT at both short and long-term follow-up, it is now widely recognised that MAT is no longer
experimental surgery. A meta-analysis by Elattar et al. reported on 44 trials that included 1136 grafts in 1068 patients, essentially showing that if patient-reported outcomes were good at 2 years postoperatively, then they could be maintained up to 20 years.

A further meta-analysis by Smith et al. of 1332 patients in 35 eligible studies reported a graft failure rate of 10.6% at 4.8 years as defined by knee replacement or graft removal. Furthermore, a complication rate of 13.9% was noted at 4.7 years, which is similar to many biological procedures in the knee.

MAT has traditionally been thought not to prevent OA; however, recent evidence from a systematic review looking at the radiographic outcomes following MAT has suggested that there is some weak evidence to support the role of MAT as a chondroprotective measure.

The most compelling data available to date are that presented by Spalding at the recent ISAKOS meeting in Shanghai, 2017. In a randomised controlled trial comparing MAT to maximised non-operative treatment, they demonstrated a statistically significant improvement in patient-reported outcomes at 2 years in favour of MAT. It remains to be seen whether this finding will remain following completion of an adequately powered study.

**SPECIFIC POPULATION**

- **Athletes:** Some recent reports have shown that MAT can provide a 70%–80% return to sport in soccer players and patients with a preinjury Tegner score of 8. However, these series comprised a low number of patients and short follow-ups. Regarding these limitations and in light of their findings, MAT could be performed in patients involved in competitive sports. However, these patients must be aware of the survival risk ratio of their transplanted meniscal allografts.

- **Children/adolescents:** Several reports have shown good outcomes with MAT in young patients. This is especially important due to their inherent high activities and the relevance of its potential chondroprotective effect. The meniscus reoperation rate and revision MAT procedures are usually low, and usually lower than in other patients, probably due to the better healing response in younger patients. MAT has shown to be a safe treatment that provides reliable results even in skeletally immature patients. However, no high-quality study has focused exclusively on a paediatric population. These data are necessary to establish a potential prophylactic indication in this specific population.

- **Advanced cartilage injury:** The outcomes after MAT may be compromised by the presence of OA and indication in this scenario should be taken with caution. Although some studies report promising results with a mean graft survivorship of 12 years in patients with advanced chondral injuries, larger series and a number of meta-analyses have all demonstrated that poorer outcomes are expected in the face of OA. Probably, in younger patients with arthritis, in whom non-operative measures have failed and no other surgical option exists, MAT can be offered as a bridging solution.

- **Concomitant procedures:** Most patients undergoing MAT have concomitant procedures performed in the same surgery. The most frequently associated procedures performed are cartilage repair/restoration, ACL reconstruction and osteotomies. In general, the outcomes of MAT with concomitant procedures are no worse than outcomes of isolated MAT. MAT and associated cartilage procedures (autologous chondrocyte implantation, osteochondral allograft, osteochondral autograft or microfractures) essentially provide improvements in pain relief, functional scores and sports level that are similar to those in isolated MAT.

- **Over 50 years old:** Age on its own should not be a formal contraindication. Ligament integrity, alignment and other concomitant injuries are the defining aspects to consider when a patient is a potential candidate for MAT. Regarding articular cartilage state, advanced bipolar injuries in this specific age group might be better addressed with metal solutions than with MAT.

### Where do we go next? Future trends

The many different techniques and attempts made to substitute the lost tissue can be classified into three categories. First is substitution with natural tissues, such as meniscus allografts, quadriceps tendon and Hoffa fat pad. The second approach is to substitute the meniscal tissue loss with tissue-engineering scaffolds, potentially with cells and specific cytokines; finally, there would be a place for prosthetic implants.

Currently, three areas of research are identified: (1) optimisation of meniscus allograft transplantation with focus on graft biology and graft extrusion; efforts to minimise extrusion by additional fixation of the graft to the bone, additional fixation of the meniscus ‘skirt’ to the tibial plateau and ‘belt’-type approaches to prevent the capsule to extrude are under current investigation; (2) better understanding of the patient-specific healing potential by diagnosing good and bad healers prior to surgery; (3) design of scaffolds and implants to substitute meniscus tissue.

MAT is considered the gold standard treatment for a young patient who has had a total or subtotal meniscectomy. Segmental defects after partial meniscal tissue resection are commonly seen in the clinical practice. However, we know little about partial substitution with biological tissues. Adding up that more patients are increasingly requesting partial substitution due to the greater awareness of the population with regard to the relationship between OA and the degree of meniscal

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**Highlights for rehabilitation**

- Non-weight-bearing to slight weight-bearing in the first month.
- ROM limited to 0°–90° in the first 6 weeks.
- Light running after the fourth month.
- Strenuous activities not recommended or only with great caution.

**Minimum outcome data set as recommended by IMREF**

- **Disease-specific score:** WOMET (Western Ontario Meniscal Evaluation Tool)
- **Region-specific score:** KOOS (Knee Injury and Osteoarthritis Outcome Score)
- **Activity score:** Marx Activity Rating Scale
- **Cost-effectiveness/utilities:** EQ-5D (EuroQol-5 dimension)
tissue loss. Different acellular scaffolds have been used in clinical practice in order to solve this problem.95 Findings to date indicate that these scaffolds promote tissue regrowth.95 Because our knowledge of the repair biology of the injured meniscus is scant, these treatment modalities are a sort of ‘injury model’ and have improved the healing processes knowledge. The tissue seen after implanting these scaffolds seems immature while comparing to the native meniscal tissue. Some translational research is now focusing how specific cells and cytokines may lead to accelerated healing.96 Interestingly enough, the mechanical characteristics of available scaffolds are not yet those of the native meniscus. The mechanical stimulus plays a key role in cell maturation and differentiation and it seems logical that a more biomechanic scaffold would derive in a more meniscus-like tissue. What we now need are studies that clarify the potential of a one-step isolation technique with bone marrow or combining these cells and ‘on the spot isolated’ primary cells; such knowledge would help obviate the costly procedure of cell culture and the two-step procedure.102

Another focus of attention for repair and healing in several clinical applications is the use of platelet-rich plasma concentrate. Unfortunately, the use of isolated recombinant growth factors is currently highly controversial and subject to high regulatory constraints. Experimental studies suggest than some of them increase patient-specific healing potential.97 102

The application of a prosthetic meniscus device is yet another area of research in the field.103 Implants of this type, however, are highly difficult to design in view of the complicated biomechanical behaviour of the meniscus.13 It is also unclear whether its fixation to the capsule and bone is necessary. A considerable amount of research is presently under way with novel biomaterials that may enable the manufacture of typical meniscus surface characteristics.

In conclusion, many different approaches to substitute the meniscal tissue loss are currently under investigation. Improvement of the specific healing capacity of each patient is an area of major interest for the tissue engineer. Finally, the ongoing research will hopefully lead to the development of an ideal material for a prosthetic device in the near future.102

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