Meniscectomy is one of the most common procedures in orthopaedic surgery, capable of returning the knee to satisfactory functionality when a meniscal tear occurs\(^1\). However over the years, several concerns have arisen about its detrimental effects on the joint status in the medium- to long-term. In fact it is nowadays acknowledged that loss of meniscal tissue permanently alters knee biomechanics and homeostasis, with secondary degenerative changes to the articular cartilage and higher risk of developing symptomatic osteoarthritis (OA)\(^2\). Hence, meniscus repair and substitution have gained significant interest.

Unfortunately, the effectiveness of meniscal repair strictly relies on the tissue quality and defect location with respect to the vascular supply; tears in the vascularised ‘red’ peripheral zone are more likely to heal, whereas the more common lesions in the avascular ‘white’ area have a poor chance of healing\(^3\). Meniscectomy is unavoidable in over 90% of cases.

In recent decades, meniscus substitution strategies have been developed to replace symptomatic loss of meniscal tissue. Meniscal allograft transplantation (MAT) and meniscus prostheses are suitable to replace a complete or subtotal loss of meniscal substance, while scaffolds have been developed for segmental meniscus defects.

Whereas MAT is a well-established procedure, with extensive literature highlighting the results in very long-term follow-up, the role and indication of repair, scaffolds and prosthesis remain more controversial. All these options are now available in order to save or replace damaged meniscal tissue, with the goal of providing early pain relief, healing of the damaged or absent tissue and prevention of secondary joint degeneration in the long term.

However, their effectiveness in terms of clinical improvement, as well as long-term chondroprotection can still be improved.

This narrative review aims to highlight the current state of the art in advancements in meniscal surgery.

**REPAIR PROCEDURES**

When surgically approaching an injured meniscus, the possibility of a repair should always be considered and several options are today available for the surgeon, from open to minimally invasive procedures.

Despite the fact that meniscal repair has become more common in recent times, the indications still remain controversial. Dehaven et al first stated the best indication for surgical repair was a tear within 2 mm...
of the peripheral junction. Later Beaufils et al extended this cut-off to 4 mm for arthroscopic repair, provided that the tear is located into the red-red zone.

Different techniques can be applied in order to perform a meniscal repair. Inside-out techniques allow most meniscal tear types and locations to be repaired with high precision. However, more recent arthroscopic all-inside techniques are now widespread due to the minor morbidity and shorter surgical time, together with comparable success rates. However, outside-in repair remains the preferred procedure for anterior horn tears.

Regardless of the technique used, current repair techniques provide stability to the tear, with a 60% complete healing rate. Meniscal repair has been shown to be associated with relatively higher complications and reoperation rates (up to 22% mean at 10 years) compared to meniscectomy in the short term. While in the long term, patients showed better outcomes and less activity limitations when a repair was performed.

**Recent advances**

Improved diagnostic tools and a thorough knowledge of biomechanics have recently drawn the attention of clinicians to particular patterns of meniscal lesions that have been misdiagnosed or underestimated in the past.

First described by Strobel et al in 1988, ramp lesions involve the posteromedial menisco-capsular or menisco-synovial junction and have been reported in 9 to 40% of ACL tears, but they have been historically under-recognised during standard arthroscopy and using MRI. Some authors consider these tears to have a high probability of healing, being in the red-red zone, whereas others highlighted the need for a surgical stabilisation due to the high mechanical stress the area is subject to. Thus, several techniques have been proposed for the arthroscopic repair of these lesions, either outside-in or inside-out, requiring an additional posteromedial portal, with satisfactory results being reported up to mid-term follow-up. However, nowadays the use of all-inside procedures is becoming the gold standard for the treatment of ramp lesions thanks to progress in specific surgical devices.

**Figure 1a:** Meniscus ramp lesions might go undiagnosed when visualised during classic arthroscopy, as illustrated with the camera through the anterolateral portal and the hook through the anteromedial portal.

**Figure 1b:** The same meniscus lesion visualised through the notch.

**Figure 1c:** Meniscus ramp lesion repaired with all-inside meniscus suture.
Another clinical entity that recently came to attention is the meniscus root lesion. It consists of a radial tear of the meniscal root, with partial or complete avulsion within 9 to 10 mm from the tibial footprint. This entity was first described in 1935 due to concomitant bone avulsion at the tibial plateau visible on X-ray, though the first modern description was in 1991. These tears can occur in either meniscus, but in 70% of the cases they are located at the posterior medial root and can be due to both traumatic or degenerative conditions. Biomechanically, the effects of posterior medial or lateral root tears have been compared to that of a total meniscectomy, with a high risk of secondary cartilage and subchondral bone conditions on the medial side and residual increased rotational instability on the lateral side. Currently, arthroscopic repair is the main indication for many of these lesions, depending on their type. The surgery can be performed inside, inside-out or outside-in for partial avulsion or those close to an intact root, whereas transosseous techniques are preferred for complete root tear reinsertion. Care should be given in case of concomitant or previous ligament reconstruction in order to avoid tunnel conflicts, otherwise the use of suture anchors has also been described to overcome this issue.

While the optimal treatment of these tears is still debated, most authors report good clinical outcomes after root tear repair. However, Chung et al – in a recent meta-analysis – pointed out that medial meniscal root repair, besides the clinical benefit, did not improve meniscal extrusion, not stopped the progression of OA.

**Augmentation techniques**

The structural healing rate after meniscus repair has been shown to be relatively low (50 to 80%), but it improves when the repair is performed in conjunction with ACL reconstruction, probably due to growth factors (GFs) and cytokines coming into the articular space from the ACL bone tunnels. For this reason, different biologic methods have been developed in order to increase the presence of growth factors and cytokines.

Bone perforations in the notch area or vascular access channels can be created to produce intra-articular bleeding. Mechanical methods such as trephination and abrasion aim at increase the vascularity at the repair site, whereas other methods involve direct growth factor delivery on-site, such as the application of synovial flaps, fibrin clots or the use of mesenchymal stem cells (MSCs).

GF-based strategies aim to enhance the limited regenerative potential related to the vascularisation pattern of the meniscus by providing angiogenic stimuli. Even though vascular endothelial growth factor is the main angiogenic GF, it is not capable of improving meniscal healing alone and a combination of GFs might be more effective.

Platelet-rich plasma (PRP) contains a high number of proteins, cytokines and different GFs. Moreover, it can be easily obtained by a sample of autologous peripheral blood through minimal manipulation. Besides different formulations and activation methods, it can be applied as a liquid product or as a gel when it is treated with activating agents. Unfortunately, few clinical data from low-level studies are available on PRP use for meniscal repair to date. A comparative study by Griffin et al failed to observe any benefit of PRP.
administration after meniscal repair, both in terms of clinical outcomes or failure rate\textsuperscript{4}. Conversely, PRP administration at the end of open meniscal repair improved clinical outcomes at 24 months follow-up in a case-control study\textsuperscript{17}.

MSCs can be harvested from various autologous sources (bone marrow, adipose tissue, muscle and synovium)\textsuperscript{18,19}. The rationale of using MSCs for meniscal treatment is to provide both cell precursors and their signalling activity on-site. Preclinical studies showed MSCs favour the repair of meniscal defects in the avascular zone, forming a meniscal-like tissue with extracellular matrix\textsuperscript{20}. Moreover, MSCs showed the ability to differentiate into meniscal fibrochondrocytes after intra-articular injection in animal models\textsuperscript{20}.

Nevertheless, very limited clinical evidence is available; Vangsness et al performed a randomised controlled trial reporting better improvement in pain than controls at 12 and 24 months after a single intra-articular injection of allogeneic bone marrow-derived MSCs following partial medial meniscectomy\textsuperscript{21}. Pak et al investigated the safety of adipose-derived MSCs administration, with no major issues. However, they reported only a single case where injecting MSCs combined with PRP was effective for a grade II tear of the medial meniscus\textsuperscript{22,23}. Combining preclinical and preliminary clinical findings, the use of MSCs shows promising results in promoting meniscal repair or post-meniscectomy regeneration, even though there is limited clinical literature due to several translational issues still to be overcome.

REPLACEMENT

Meniscus allograft transplantation

MAT was first introduced in 1984, with the ideal indication of treating symptomatic subtotal or total meniscectomies in young to middle-aged patients, with proven clinical efficacy in the long term – even in combination with other knee procedures (ACL reconstruction, osteotomy, cartilage repair).

The re-operation rate after MAT is however relatively high, with as many as 30 to 46\% of patients requiring subsequent surgery\textsuperscript{25}. However, it has been highlighted that most of the re-operated patients undergo surgical debridement only. Concerning functional outcomes, 76\% of the patients returned to light low-impact sports in a series by Noyes et al\textsuperscript{26} and most authors raise concerns against the application of MAT in active athletes\textsuperscript{27}.

The graft has abnormal MRI appearance in more than 75\% of cases, but this feature seems not to correlate with any clinical parameter. With regard to OA progression, up to 58\% of the patients showed stable features on X-ray evaluation, while a slight-to-moderate worsening was observed in the remaining ones between 5 and 15 years of follow-up. Overall survival rates after MAT were reported as 93.5\% at 3 years and 95\% at 5 years and 80\% at 10 years in different studies\textsuperscript{28}.

This time-dependent trend suggest meniscus allograft might represent an effective but temporary solution for post-meniscectomy pain.

Scaffolds

Meniscus scaffolds are three-dimensional biocompatible structures, capable of supporting meniscus-like fibrocartilaginous tissue regeneration in segmental meniscus defects. Two constructs for meniscal replacement are available on the market: the first is made of bovine collagen (collagen meniscus implant: CMI\textsuperscript{®}, Ivy Sports Medicine GmbH, Gräfelfing, Germany), the second more recent one, consists of a synthetic polyurethane-based material (Actifit\textsuperscript{®} orteq Sports Medicine, UK)\textsuperscript{29}.

The indication involves a segmental symptomatic loss of meniscus tissue, with intact anterior and posterior attachments, and intact rim over the entire circumference in order to allow a stable implant fixation.

The surgical technique is similar for both the devices, involving the arthroscopic resection of the damaged tissue and subsequent implantation of a custom-sized, porous material, which is finally sutured to the meniscal rim and capsule using standard inside-out or all-inside sutures\textsuperscript{29}. Both the implants available for clinical use, either based on collagen or a polyurethane,
showed promising short-term clinical results and stable satisfactory outcomes up to mid- or long-term evaluation. However, the MRI appearance at follow-up raised several concerns in both cases, showing the implants were reduced in size, with a hyperintense signal in most cases. On the other hand, the clinical significance of these findings is still unclear.

These scaffolds for meniscal replacement have shown to provide pain relief and symptoms improvement for the treatment of painful segmental meniscal defects. Several limitations emerged in terms of quality of the regenerated tissue and also about the hypothesised chondroprotective action. Longer term studies are necessary to fully understand the potential of these implants for wider use. Even though augmentation strategies are under investigation, several translational issues currently limit their clinical use.

**Prosthesis**

To this purpose, a new implant was recently conceived in order to fulfil the need for treatment of chronic middle-aged patients with a medial post-meniscectomy syndrome. NUsurface® (Active Implants Corp., Memphis, TN, USA) is a non-anatomically shaped artificial meniscus composed of reinforced polycarbonate-urethane, solely designed for medial meniscus replacement. Preliminary in-vitro experiments confirmed the ability of load distribution under static loading. A subsequent preliminary trial in a meniscectomised sheep model showed good materials properties but mild cartilage degeneration after the implantation of this device.

The only report on a clinical pilot study showed close-to-normal kinematic properties in the knees of three patients after implantation, but more extensive clinical trials are currently ongoing (trial number: NCT01712191).

**CONCLUSIONS**

The meniscus is a crucial player in knee homeostasis and its preservation is now considered necessary to obtain satisfactory clinical results, above all in the long-term follow-up to avoid the future onset of arthritis. Nevertheless, repair procedures result in variable outcomes. Several strategies to enhance the healing potential of the meniscus have been proposed, via the delivery of ‘factors’ or ‘agents’ to promote tissue healing, particularly in the avascular zone of the meniscus, so that many more patients might benefit from procedures aimed at the preservation of meniscal tissue. Even when a repair is impossible or failed, different innovative options are now available in order to replace damaged or lost meniscal tissue, with the aim of allowing satisfactory clinical improvement to patients and delaying the need for knee arthroplasty. However, the role of any of these procedures in terms of chondroprotection is questionable and overall long-term outcomes can still be improved.

References available at www.aspetar.com/journal

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