Alternatives to Meniscus Transplantation Outside the United States

19

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Collagen Meniscal Implant

Indications
- Age less than 55 years
- Pain after partial meniscectomy

Contraindications
- Osteoarthritis (> III)
- Pain after total meniscectomy
- Allergy to implant material
- Infections
- Rheumatoid diseases

Controversial
- Age more than 55 years
- Irreparable acute lesions with meniscal loss >25%

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Case Study

A 45-year-old man complained of pain and anterior instability of the left knee following a knee sprain during physical activity that occurred 6 months earlier. Physical examination revealed full range of motion (ROM), positive Lachman and anterior drawer tests, and tenderness at the medial rim of the joint. X-rays were negative for bone abnormalities and joint malalignments, while magnetic resonance imaging (MRI) showed a complex tear of the posterior horn of the medial meniscus, complete anterior cruciate ligament (ACL) rupture, and a chondral lesion of medial femoral condyle.

At arthroscopy, all the lesions were confirmed (Fig. 19.1a, b) and collagen meniscal implant (CMI) was performed after partial meniscectomy, involving a 4-cm portion of the medial meniscus. An ACL reconstruction with hamstrings was then carried out. The chondral lesion measured 4 cm^2. A cartilage specimen was harvested from the superomedial edge of the femoral trochlea and sent to laboratory for chondrocytes expansion. No complications occurred in the postoperative period. Five months after the first operation a matrix-induced autologous chondrocyte implantation procedure (Genzyme, Boston, MA, USA) was performed to treat the chondral defect. In this technique, a type I–III collagen membrane acts as scaffold for supporting the cells. Fixation of the membrane on subchondral bone is achieved using exclusively fibrin glue. At 4-year follow up, the clinical and functional results were good

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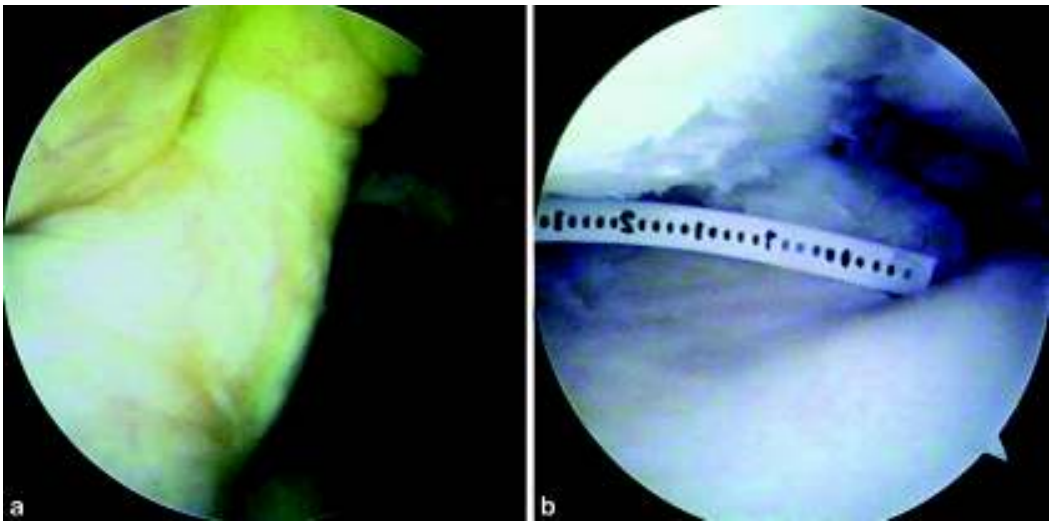

Fig. 19.1 **a** Anterior cruciate ligament (ACL) tear. **b** Full thickness chondral defect of the medial femoral condyle and posterior horn irreparable meniscal lesion

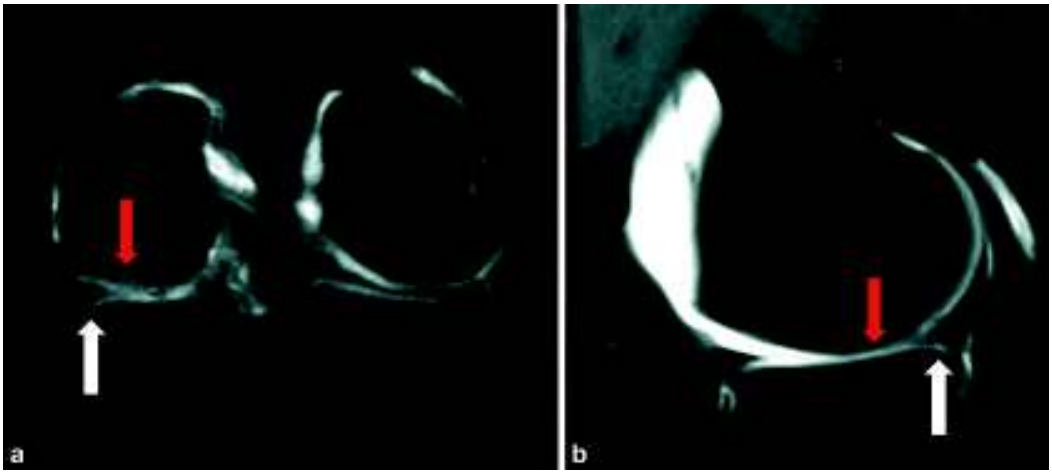

Fig. 19.2 FSE Fat-Sat (fast spin echo fat-suppressed) Arthro-magnetic resonance imagings (MRIs). **a** coronal, **b** sagittal planes. Collagen meniscal implant (CMI) dimensions remained unchanged with a signal gradually resembling the meniscal fibrocartilage (*white arrows*). The chondrocyte implant remained in site and showed a hyaline-like signal with good restoration of the articular surface (*red arrows*)

and MRI showed integration of the meniscal and cartilage implants (Fig. 19.2a, b).

Actifit™

Indications

- Irreparable medial or lateral meniscus defect due to previous partial meniscectomy, which causes pain and functional limitation
- Body mass index (BMI) ≤ 35 kg/m^2

- Cartilage lesion up to grade III of the International Cartilage Repair Society (ICRS) classification
- Meniscal loss more than 25%.

Contraindications
- Posterior root lesion
- Total meniscectomy or insufficient native tissue either on the anterior or the posterior horn
- Cartilage lesions above grade III of the ICRS classification
- Untreated knee instability or varus/valgus deformity
- Infections
- Rheumatoid diseases
- BMI > 35 kg/m^2.

Controversial There is no indication yet on acute irreparable meniscal lesions, since there are no data available on chondroprotective effects of the scaffold on the long run.

Synopsis: Author's Recommendations

Technique
- Partial meniscectomy until the red zone
- Bleeding stimulation of the tissue with shaver and/or a needle
- Accurate preparation of the scaffold for a precise contact with the native meniscal tissue
- Suture of the scaffold in this order: posterior, anterior, then the central part.

Avoid
- Implant the scaffold in presence of a posterior root lesion
- Leaving too much native tissue in the site of the lesion: it can compromise the vascular ingrowth.
- Suture the scaffold in its central part as first: it may cause a shortening of the device.

Case Study

A 48-year-old healthy male, very active in sports (bicycle and running), presented with a history of increasing medial knee pain within daily activities. He had previously undergone a partial medial meniscectomy with complete resolution of the pain. Physical examination demonstrated BMI of 30 kg/m^2, good muscle tone of either of the lower extremities and varus alignment. Radiographs showed well preserved medial joint space and a weight-bearing mechanical axis that fell through the middle half of the medial tibial plateau, consistent with varus alignment of 8°. His MRI demonstrated medial meniscal deficiency and a chondral defect of the medial side of the knee. After discussion of treatment alternatives he chose to proceed with the Actifit^{TM} scaffold implant to address the meniscal deficit and concurrent medial opening wedge high tibial osteotomy (HTO) for his medial compartment overload due to the meniscal deficiency (Fig. 19.3a, b, c). One year after surgery he had the plate used for the HTO, removed (VS Dinafix-Biomet, measure 11.5): the knee was scoped and we found good but incomplete integration of the scaffold inside the native knee (Fig. 19.4a, b, c).

He is currently 2 years' post-op and is functioning well with little-to-no pain within his activities of daily living and sport.

NUsurface®

Controversial Focal grade IV chondral lesions: Some patients, especially in the first-in-man series, have been treated successfully even in presence of a focal grade IV lesion without condyle deformity.

Synopsis: Author's Recommendations

Technique First step: Arthroscopy: Joint debridement and medial meniscectomy leaving about 3 mm of the remnant tissue. Do not treat focal cartilage lesion, just make smooth edges in order to facilitate the gliding of the device.
Second step: Open surgery: if trial implant lifts anteriorly in maximum flexion, use the bigger size. Fluoroscopic control of the trial device is possible.

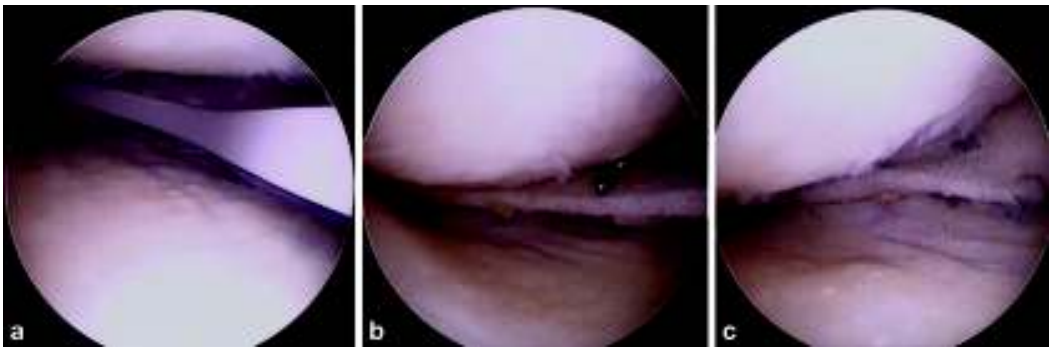

Fig. 19.3 **a** Medial-side cartilage degenerative lesion: intrarticular measurement of the length of meniscal loss. **b** Intrarticular positioning of the Actifit™. **c** Actifit™ after completion of sutures

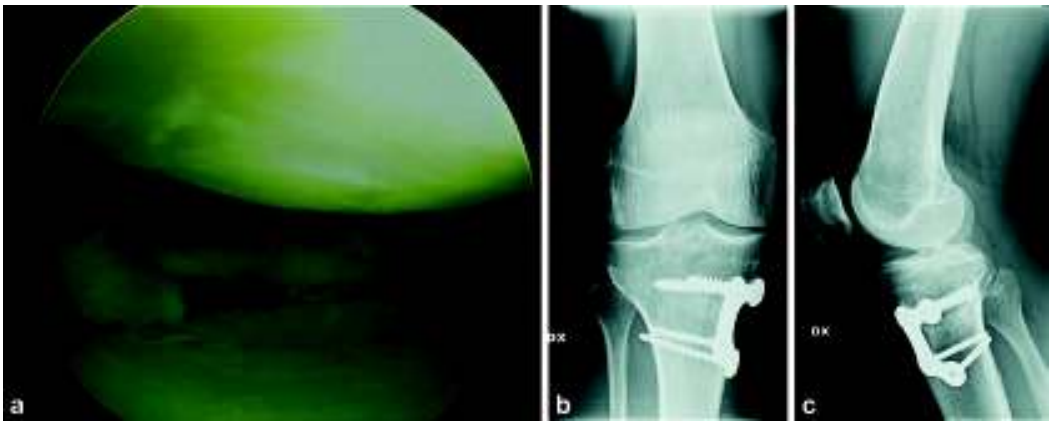

Fig. 19.4 **a** Actifit™ at the posterior horn 1 year after implantation: good integration but not complete. **b**, **c** X-ray in AP (**b**) and lateral (**c**) one post-HTO and Actifit™ implantation

Avoid Implantation of the device in case of insufficiency of the posterior root: higher risk of posterior luxation.
Open release of medial structures.

Case Example

A 64-year-old male patient was treated using the NUsurface® Meniscus Implant on May 12, 2008.

No previous history of arthroscopic procedure or other knee operations. The patient's main complaint was medial pain during daily activities (see questionnaires scores in Fig. 19.5). The MRI showed a complex tear and a calcium pyrophosphate deposition disease in the posterior horn of the medial meniscus, intact lateral meniscus, and ligaments. Standing bipodal X-rays showed normal axis.

Grade III Outerbridge (OB) cartilage damage in the medial compartment was diagnosed by both MRI and arthroscopy. A standard arthroscopy procedure with joint debridement and total meniscectomy was performed. Some of the deep fibers of the medial collateral ligament (MCL) were released. An ~8 cm incision adjacent to the patellar line was made, through which a trial implant was inserted. The trial implant was tested intraoperatively for ROM and potential impingement (via fluoroscopy). Finally, the adequately sized NUsurface® device was implanted.

Six weeks after the surgery, knee pain was lower (Knee injury and osteoarthritis outcome score (KOOS) pain = 53), but not yet significantly

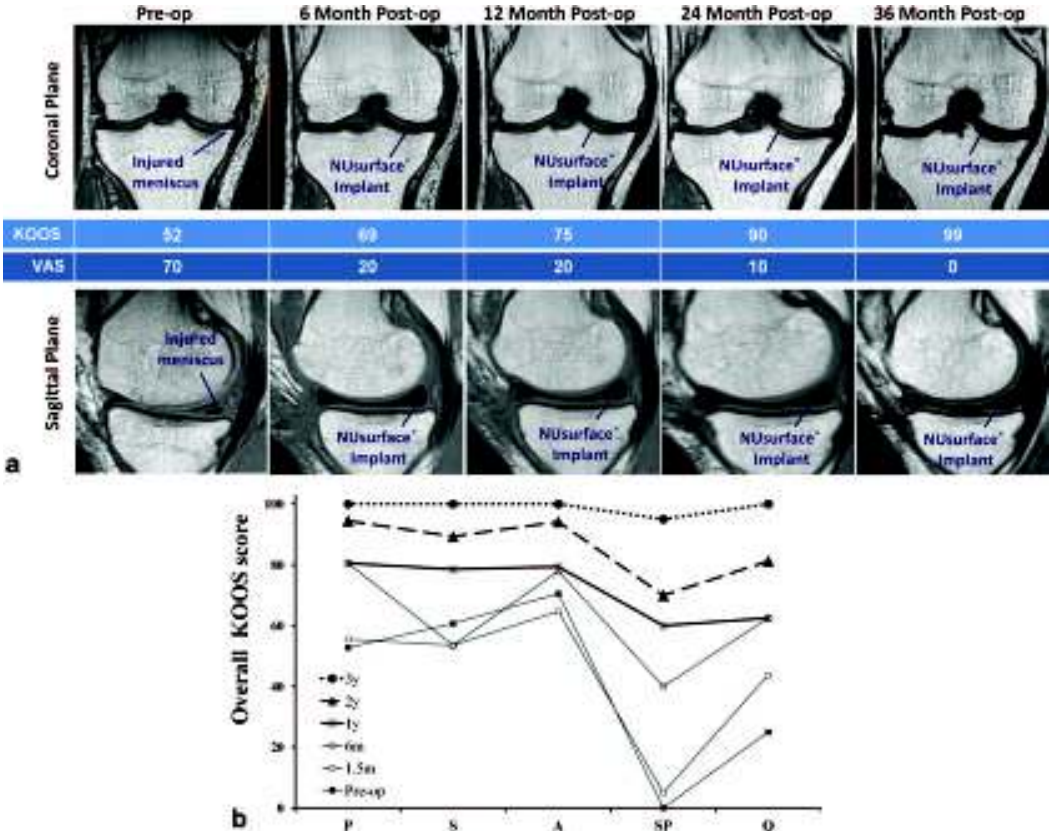

Fig. 19.5 **a** Comparison of MRI images with questionnaires score for the first 36 months after NUsurface® implantation: reduction of the bone oedema underneath the medial tibial plateau with no other changes. **b** Evolution of Knee injury and osteoarthritis outcome score (KOOS) scores for the first 2 years: actually, at 4 years' follow-up, KOOS score overall including sport subscales is 99; the VAS is 0 and the WOMAC is 99

improved when compared to the preoperative score (KOOS pain =56). Before the operation, pain occurred in strenuous activities including gait, whereas after 6 weeks, pain occurred only when climbing stairs or bicycling. Remaining pain was focused in the posterior portion of the knee. Gait was normal, but slow when bearing load on the operated knee. ROM was still limited (extension gap of 8°).

Six months after surgery, pain had almost disappeared. Even the Sports KOOS subscale had improved from 0 pre-op to 40.

One year post-op, the patient had no pain at all, even under weight-bearing. The Sports KOOS subscale had increased to 60. He could easily bear weight, riding a bicycle, or even play soccer (Fig. 19.5a, b).

In all recent follow-up visits (2, 3, and 4 years), the KOOS pain score was >90. The Sports KOOS score was >70. No limitations in ROM were observed.

Introduction

Background Fortunately, the "dogma" of total meniscectomy being the only effective treatment for meniscal injuries has been abandoned. However, although research and development of new and more efficient ways of treating meniscal damage has made considerable progress, the ultimate goal to preserve as much native meniscal tissue as possible through repair or other means is often not achieved. Meniscal repairs are used

to treat meniscal tears in <15% of patients in most studies (obviously dependent on the age group and associated pathology, e.g., ACL tear). The other 85% of meniscal tear treatments (partial meniscectomy) are "partial" meniscectomy. From a biomechanical standpoint, these "partial meniscectomy" patients are closer to meniscectomy in function than an intact meniscus [1]. As a result, there are a large number of patients without functioning menisci and a certain percentage will develop symptoms secondary to the altered stress in the ipsilateral compartment. (See Chap. 8 for additional information.)

Current State of Art New approaches to meniscal tear fixation (primarily arthroscopic) are continuing to be developed to improve meniscal tear healing [2]. A large number of devices for the fixation and repair of damaged menisci are available from the orthopedic sports medicine industry [3]. Nevertheless, the functional outcomes remain largely unchanged from earlier repair techniques (open or inside out with vertical mattress suture). Due to the meniscal tissue nature, and its limited healing characteristics, none of these methods proved to guarantee long-term functional recovery and/or the prevention of osteoarthritis development [4].

In addition to mechanical fixation, which is a necessary first step to provide a basis for healing, there is active research to elucidate new ways to stimulate tissue healing through biologic means. The potential of platelet rich plasma, cytokines, and growth factors to improve healing has been examined [5, 6]. Another approach has been cell-based technologies and the application of tissue engineering techniques in meniscal regeneration [7]. While potentially promising, none of these approaches have reached clinical relevance to date.

Meniscal transplantation is another option for treating a meniscal deficient knee [7]. In certain situations, these transplants can almost normalize load transmission in these knees, and thus potentially protect articular cartilage from accelerated degeneration as shown by Cole et al. in the laboratory [1]. However, there is only weak evidence that meniscus allograft transplantation does indeed prevent such cartilage degeneration in the long term; for example, Verdonk et al. [8, 9] reported that only 35% of patients did not have degeneration 10 years after meniscal transplantation, however, this was not a controlled study (see Chap. 18 for the technique of meniscal transplantation).

In recent years, possible alternatives to meniscus transplantation have been proposed. These technologies may be roughly divided into two categories: (1) biological or biomimetic scaffolds and (2) nonbiological devices (i.e., meniscal substitutes). The first category consists of biological constructs that serve as scaffolds to promote the ingrowth of pluripotential cells that could potentially differentiate into fibromeniscochondrocytes. These products currently are Menaflex™, (or CMI, ReGen Biologics, Inc., Hackensack, NJ, USA) [10], and Actifit™ (Orteq Ltd, London, UK) [11]. While the Menaflex is not load-bearing, Actifit™ is designed to be load-bearing and provide improved knee biomechanics (stress distribution) until new meniscal tissue has formed.

In the second category, biologically inert materials are inserted into the compartment and are immediately load-bearing, but do not have biological ingrowth properties. These may also be termed interpositional arthroplasties. Metal alloy interpositional arthroplasties include the iForma™ (Conformis Inc., Burlington MA, USA), and the UniSpacer™ (Zimmer Inc., Warsaw IN, USA), which is no longer on the market [12, 13]. Alternatively, the interpositional arthroplasty may be made of a polymer, such as polycarbonate-urethane (PCU) (NUsurface®, Active Implants Corp., Memphis TN, USA, investigational status) [14]. The NUsurface® at present is solely designed for the medial compartment. The goal of this implant is to provide a re-equilibration of the compartment stress by improving contact area and to an unknown extent by increasing the joint space, thus changing alignment and further decreasing loading. With decreased stress, it is suggested that the implant will reduce pain, restore mobility, and possibly even prevent further cartilage damage.

Fig. 19.6 Collagen meniscus implant (CMI). The semicircular shape and triangular section like a normal meniscus is evident

Collagen Meniscus Implant

The Menaflex collagen meniscus implant, formerly known as CMI, is a tissue engineering product, originally described in 1992 [10]. It was designed for the management of irreparable meniscal tears or previous partial meniscectomy. The intent was for the implant to stimulate regeneration of meniscal-like tissue and secondarily to prevent degenerative joint changes in the knee [10]. CMI is composed of a three-dimensional type I collagen network derived from bovine Achilles tendon, and enriched with glycosaminoglycans (GAGs), including chondroitin sulfate and hyaluronic acid, with the goal of stimulating cellular ingrowth. It is processed chemically and physically to remove molecular antigens and noncollagenous materials. The shape is similar to the human meniscus and the materials used are biocompatible (Fig. 19.6) [10, 15].

In vitro studies showed that fibroblasts can migrate inside the scaffold, which enhances cells proliferation and extracellular matrix production [10]. In animal studies, CMI demonstrated biocompatibility and resorption times ranging from 9 to 12 months [10]. These data were confirmed by clinical feasibility studies, which showed the formation of a meniscal-like structure without any cartilage damage and immunologic reaction [15, 16]. In the clinical setting, the variables may be schematically divided into two groups: biological factors, such as age of the patient, degree of joint degeneration, etc., and mechanical factors, such as the size of the lesion, any limb malalignment, and knee instability that represent relative contraindications to the CMI if not corrected before and/or at the time of surgery. The results at medium- and long-term follow-up are promising if correct indications are respected and patients are compliant with the rehabilitation program [17–20].

Surgical Technique

A CMI is performed arthroscopically, using traditional anterolateral and anteromedial portals. After thorough standard arthroscopic evaluation of the knee joint, only the irreparably damaged tissue is removed. The periphery of the segmental defect should have healthy tissue in the red–red or red–white zones. After debridement, the meniscal defect is sized using a dedicated measuring rod, and the CMI is measured and trimmed to fill the defect. Trephination of the remnant and perimeniscal synovial abrasion of the adjacent capsule are performed with the goal of augmenting a "healing response" to potentially augment cellular invasion of the implant.

CMI is introduced through an arthroscopic cannula. For visualization, a "pie crust" partial release of the MCL may be performed by trephination of the ligament with a spinal needle. The scaffold is sutured to the meniscal remnant using 2-0 nonabsorbable sutures with a standard all-inside, inside-out, or outside-in technique. Vertical mattress sutures are used for the body of the implant, and horizontal mattress sutures are used to secure the CMI to the posterior horn root and the remaining body of the meniscus, anterior to the segmental defect. The implant stability is tested with a probe after suturing (Figs. 19.7, 19.8, and 19.9).

Rehabilitation

The knee is kept in extension in a brace for 6 weeks. The patient is immediately allowed to perform continuous passive motion 3–4 times daily: flexion should not exceed 60° for 4 weeks

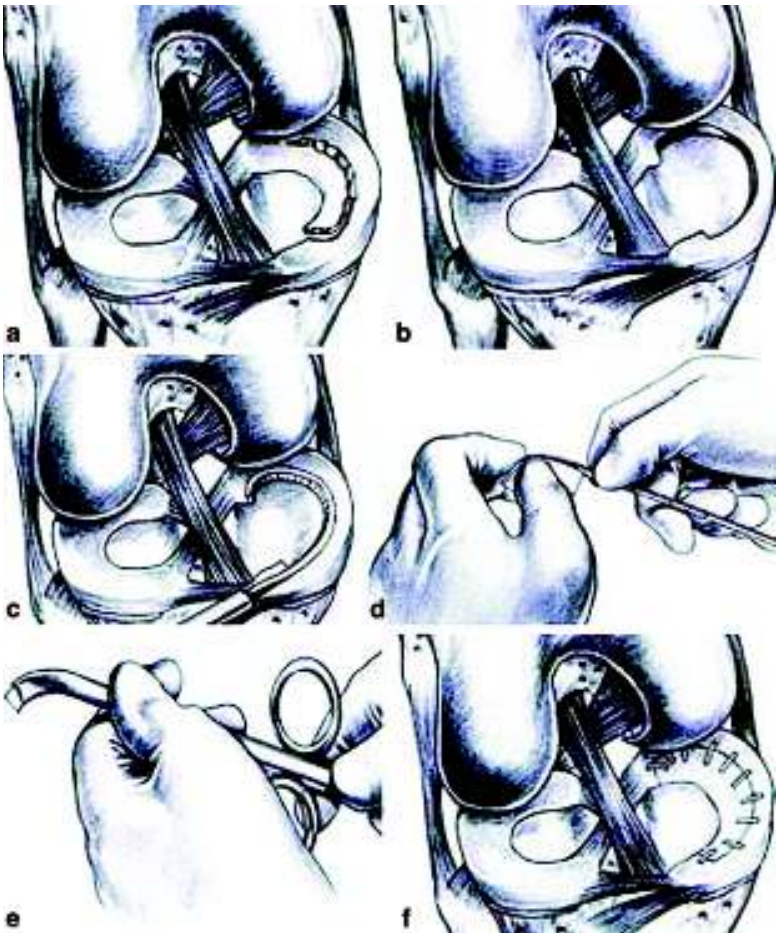

Fig. 19.7 Collagen meniscal implant (CMI) surgical technique. **a** Irreparable meniscal lesion. **b** Debridement of the lesion. **c** Measurement of the meniscal defect using a dedicated rod. **d**, **e** CMI is introduced in an arthroscopic cannula. **f** Scaffold sutured to the meniscal stump

and 90° until the seventh week. During the first 6 weeks, weight-bearing is not allowed, and patients walk using crutches. Partial weight-bearing is allowed 6 weeks after the operation and full weight-bearing 2–3 weeks thereafter. Return to unrestricted sport activities is usually allowed at 6 months.

Clinical Experience

In a systematic review, Harston et al. [21] reported the results of CMI focusing on its efficacy to improve patient function, symptoms, and activity level. A total of 520 patients (men = 428; women = 92; 17.7% women) 38.2 ± 3.7 years of age were selected. A total of 321 subjects (men = 263, women = 58; 18.1% women) received a CMI. The follow-up time was 46.6 ± 39.9 months (range = 6–135 months). The authors pointed out the importance of correcting any comorbities before CMI implantation. Overall, 41.1% of patients had concomitant procedures, such as ACL reconstruction, HTO, microfracture, autologous chondrocyte implantation, or matrix-induced autologous chondrocyte implantation. The authors concluded that knee function, symptoms, and activity level generally improved following CMI use, but poor research report quality was evident. They highlighted that additional well-designed long-term prospective studies are needed to better determine knee osteoarthritis prevention efficacy and appropriate patient selection.

Studies generally reported improved patient knee condition, symptoms, and activity level at

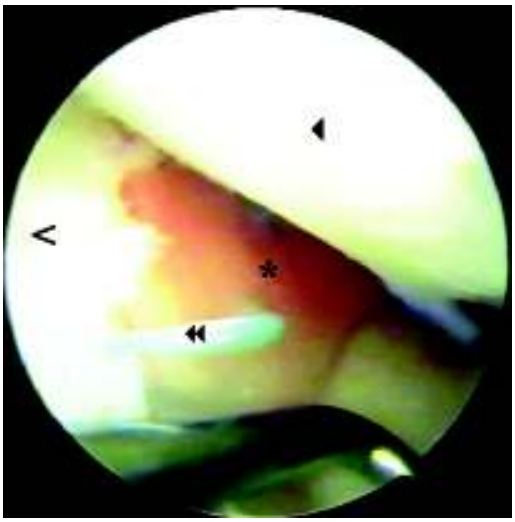

Fig. 19.8 Final arthroscopic view of CMI after implantation: (*) implant, (<) residual native meniscus, (◀) femoral condyle, and (◀◀) nonabsorbable suture

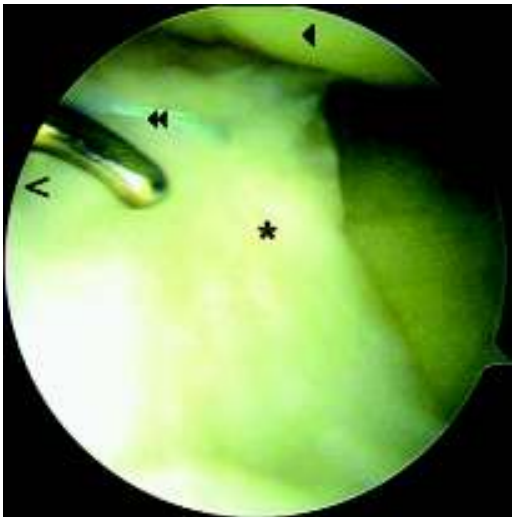

Fig. 19.9 Appearance of the implant at 6 months: (*) implant, (<) residual native meniscus, (◀) femoral condyle, and (◀◀) nonabsorbable suture

last follow-up based on the Lysholm Knee survey or the Tegner Activity Scale [15, 17, 19, 20, 22–25]. In a prospective randomized trial on 311 patients with a mean of follow-up of 59 months (range, 16–93 months), Rodkey et al. [19] reported the results of patients receiving a CMI compared to patients treated with partial medial meniscectomy alone. The mean Tegner Index values after CMI improved by 42 and 41%, respectively, in the chronic and acute patient groups, compared to 29 and 41% improvements among the chronic and acute patient groups that underwent partial medial meniscectomy alone. The authors concluded that CMI implantation allowed patients with a chronic injury, that had been treated with multiple operations, to regain as much of their preinjury activity level as patients with an acute injury, who had lost much less of the meniscus at the time of the index surgery (63% loss in the chronically injured patients who received the CMI compared with 41 and 49% loss in the acutely injured controls and patients who had received a CMI, respectively). With a minimum 10-year follow-up, Zaffagnini et al. [20] reported a mean of 75% Tegner Index value improvement among their CMI patient group compared to a mean of 50% improvement among 33 patients that underwent partial medial meniscectomy alone. Studies reporting on standard [20, 26] or patient self-reported [24–26] International Knee Documentation Committee (IKDC) survey scores demonstrated improvements ranging from +22.7 to +50.5 points, or by at least one grade by 24 months postsurgery, with Zaffagnini et al. [20] reporting at least one grade improvement by 135 months postsurgery. Zaffagnini et al. [26] also reported Cincinnati Knee Rating Scale (CKRS) results that improved from presurgery levels (240±29) to 404±35 (+164 points), 405±35 (+165 points), and 391±39 (+151 points) at 12 and 24 months and 6.8 years postsurgery, respectively. In their single case report, Ronga et al. [24] reported CKRS score improvement from a presurgery 2/10 to 7/10 at 24 months postsurgery. Using an activity score (1=strenuous activity, 2=moderate activity, 3=light activity, 4=sedentary, and 5=unable to perform sports activity) of their own design, Stone et al. [16] reported that presurgery levels of 3.0±0.5, improved to 2.4±0.5 (+0.6) at 6 months, and to 2.2±1 (+0.8) at 12 months postsurgery.

Studies that performed second-look arthroscopy with or without biopsy generally observed meniscus-like fibrocartilaginous tissue regeneration [15, 16, 26] with increasing maturity at

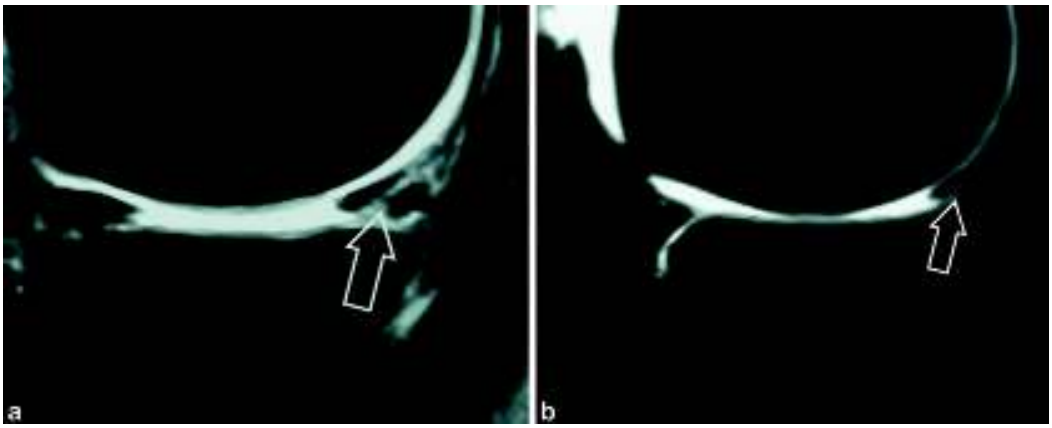

Fig. 19.10 Magnetic resonance imaging (MRI) (T2/DP sagittal images with fat suppression), by courtesy of Genovese. **a** 6 months postoperatively, the implant shows a nonhomogeneous signal (*arrow*) and appears in continuity with the capsule. **b** Control at 2 years: the signal appears more homogeneous (*arrow*), but the implant is decreased in size

longer follow-up. Bulgheroni et al. [17] reported no Kellgren–Lawrence grade changes (0=normal, 4=severe osteoarthritis) (n=18, 64.3%), or slight increases to grade 2–3 (n=9, 32.1%), or grade 4 (n=1, 3.6%) at 60 months postsurgery. Rodkey et al. [15] reported no noteworthy changes in tibiofemoral joint space or axial alignment, and no Fairbanks progression at 24 months postsurgery. Steadman et al. [25] reported that at both 24 months and 5.8 years postsurgery, tibiofemoral joint heights were unchanged in 3/8 (37.5%) of patients that received a CMI, decreased <0.5 mm in 3/8 (37.5%) of patients, and increased >0.5 mm in 2/8 (25%) of patients. Stone et al. [16] in their longitudinal case series reported no tibiofemoral joint space height changes at 36 months following CMI surgery. Zaffagnini et al. [26] reported that at 24 months following CMI implantation, tibiofemoral joint space height was unchanged in 6/8 (75%) of patients, but decreased by 1 mm in 2/8 (25%) of patients. At a mean of 135 months follow-up post-CMI surgery, Zaffagnini et al. [20] did not observe significant medial joint line narrowing compared to the contralateral knee in study group patients, while the partial medial meniscectomy control group demonstrated a 2.2±1.6 mm reduction in the involved joint space. Using MRI techniques, Bulgheroni et al. [17] reported that original CMI size decreased in 60.7% (n=17) of patients at 24 months postsurgery, and second-look arthroscopy performed in four patients at 12, 18, 36, and 60 months (one patient at each interval) revealed a new tissue complex that was smaller than the original implant. Genovese et al. [22] reported that 87.5% (35/40) of subjects had no CMI size reduction at 6 months postsurgery; however, this percentage decreased to 82.5% (33/40) and 56.3% (9/16) at 12 and 24 months postsurgery, respectively (Fig. 19.10). Biopsies confirmed progressive (25–90%) CMI size reduction over this time period [22]. Rodkey et al. [15] reported decreased CMI size at 6 weeks postsurgery with a smaller new tissue complex than a normal meniscus. However, they did not observe further size changes at 12 months postsurgery. Several studies [10, 16, 17, 19, 20, 22, 25, 26] reported progressively decreasing MRI signal intensity with fibrocartilaginous meniscal-like tissue maturation; however, Zaffagnini et al. [26] also reported myxoid degeneration at the CMI healing site in five patients at 24 and 72 month follow-up, and less tissue volume than at CMI surgery. More recently, with a minimum follow-up of 10 years, Zaffagnini et al. [26] reported an MRI signal compatible with myxoid degeneration in >50% of their study group. Rodkey et al. [15] reported 77% mean original meniscal defect filling at 12 months postsurgery. In a later follow-up study, Steadman et al. [25] reported that the original meniscal defect was 69% filled at 5.8 years postsurgery. Using

biopsies, Rodkey et al. [15] and Steadman et al. [25] observed meniscus fibrochondrocyte-like cells in the CMI of all subjects in their case series. In their later work, they reported that all CMI recipients showed evidence of newly developing fibrochondrocytic matrix formation [19]. Using electron microscopy, Reguzzoni et al. [23] observed parallel lacunae walls with collagen fibrils, blood vessels, and fibroblast-like cells at 6 months following posterior horn CMI use in four subjects. No inflammatory cells were detected [23]. Stone et al. [16] reported that between 3 and 6 months postsurgery the CMI was gradually replaced with immature collagen. In a single case study using second-look arthroscopy, Ronga et al. [24] reported that blood vessels and collagen fibrils were evident within the CMI at 6 months postsurgery.

Harston et al. [21] also reported on the quality of articles published according to the Modified Coleman Methodology Score. This score, designed to validate research report methodological quality (0 = lowest quality, 100 = highest quality), revealed a wide ranging, but generally low research report quality (67.1 ± 18.6, range = 29–97). The factors which showed greatest variability were study size, description of postoperative rehabilitation, procedures for assessing outcomes, and description of the subject selection process.

Actifit™

Actifit™ by Orteq Bioengineering Ltd. (London, UK) has improved early biomechanical properties and handling properties when compared to CMI. Actifit™ which received a CE mark in July 2008, is a biodegradable, synthetic acellular scaffold composed by two components, a polyester (poly-ε(epsilon)-caprolactone = soft segments) and polyurethane (= stiff segments) (Fig. 19.11). Animal studies performed in the 1980s examined different polymers as potential material for meniscal replacement. From those studies, a set of requirements for an optimal implant was established. These requirements include pore size, porosity, rate of degradation, degradation products, mechanical properties, and ease of use in an arthroscopic procedure [11]. Once implanted in the vascularized portion of the meniscus, the scaffold provides a three-dimensional matrix of interconnected pores for vascular ingrowth [27].

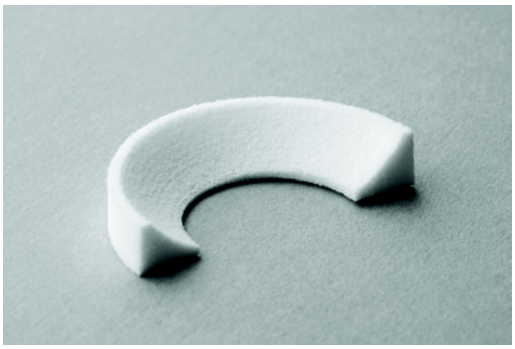

Fig. 19.11 Actifit™ meniscus implant: available in two configuration, medial and lateral. It's a biodegradable, synthetic acellular scaffold composed by a polyester (poly-ε(epsilon)-caprolactone = soft segments) and polyurethane (= stiff segments)

Biodegradation starts in the presence of water through hydrolysis of the ester bonds in the poly-ε(epsilon)-caprolactone. This process is estimated to take between 4 and 6 years. The polyurethane components are more stable and are not expected to degrade extracellularly, but rather to be phagocytized by macrophages or giant cells, which finally leads to degradation [28, 29]. Preclinical studies in dogs have shown complete infiltration of the porous structure after 3 months and complete integration with periphery capsule after 6 months [30]. The Actifit™ is available in two configurations; medial and lateral.

Surgical Technique

Standard anterolateral and anteromedial portals are used; a transpatellar portal can be useful in more difficult cases. Typically, a leg holder with a lateral support on the central third of the thigh for valgus stress aids in visualization. The first step is to verify whether the remnant meniscal tissue is sufficient to hold the scaffold: intact anterior and posterior horns and enough tissue (2 mm remnant) of the meniscal rim for the Actifit™ ingrowth. For the lateral meniscus, it is mandatory

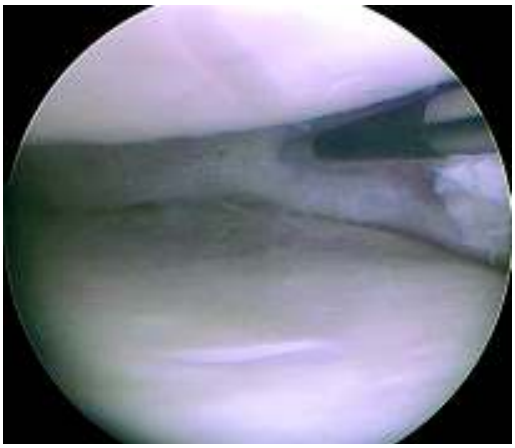

Fig. 19.12 Preparation of the meniscal bed for the Actifit™: debridement of the remnant tissue deeply to the vascular red-zone spur with a spinal needle

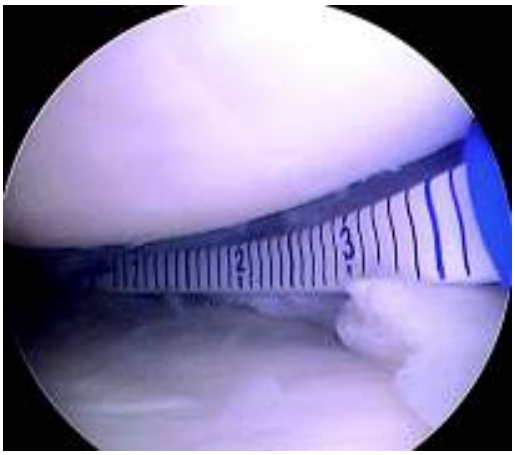

Fig. 19.13 A special ruler with its guide, included in the Actifit™ kit, is used for the measurement of the defect length

to have an intact meniscal bridge across the popliteal hiatus to ensure a proper fixation of the scaffold and, subsequently, proper ingrowth.

The remnant tissue is excised to the vascular red-on-red zone or into the red-on-white zone similar to the Menaflex preparation, which includes perimeniscal synovial stimulation and trephination (Fig. 19.12).

After meniscal preparation, the defect is measured with a special ruler and a guide supplied in the Actifit™ kit. The measurement is taken along the inner margin of the defect (Fig. 19.13).

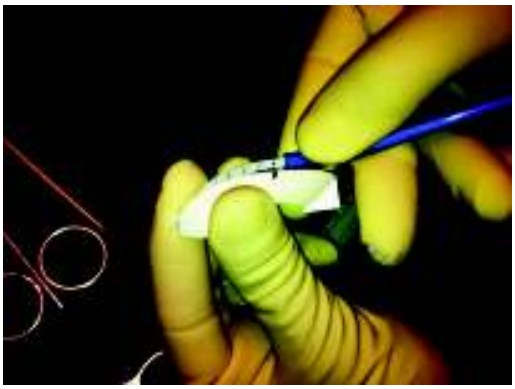

Fig. 19.14 Oversizing the length of the scaffold is necessary because the sponge-like consistency of the material reduces its volume after suturing

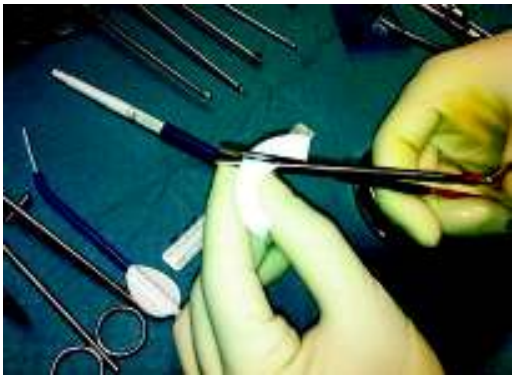

Fig. 19.15 The anterior cut is made at an angle of 30–45° for a better fit into the native meniscus cut at the same angle

The Actifit™ is then tailored to fit the meniscal defect using a scalpel to make a sharp margin following two main rules:

1. Oversizing the length by 3 mm for defects <3 cm, and by 5 mm for defects (3 cm; this is necessary because of the sponge-like consistency of the material, which reduces its volume after suturing (Fig. 19.14).
2. The anterior cut of the Actifit™ is made at an angle of attack of 30–45° in order to allow a perfect fit into the native meniscus cut at the same angle (Fig. 19.15).

The Actifit™ (clamped on its posterior part) is inserted into the joint through an enlarged anteromedial or anterolateral portal (for medial and lateral meniscal deficit, respectively), and

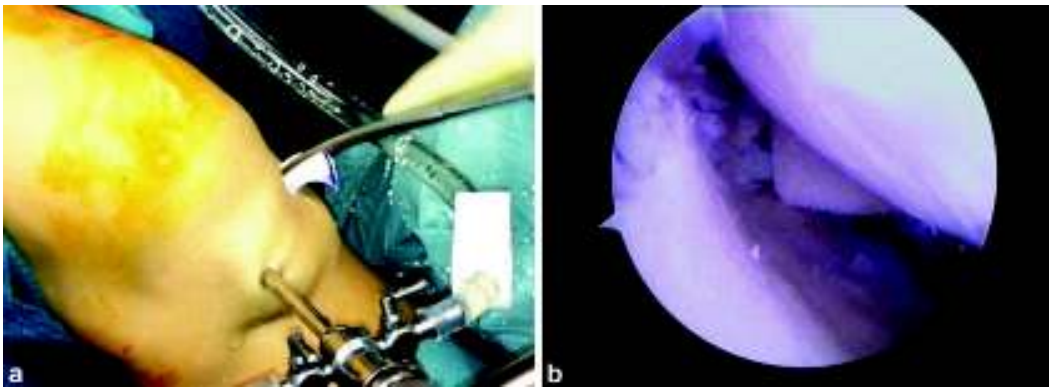

Fig. 19.16 **a** Intrarticular insertion of the device clamped on its posterior part. **b** Good fit with the remnant of the posterior horn

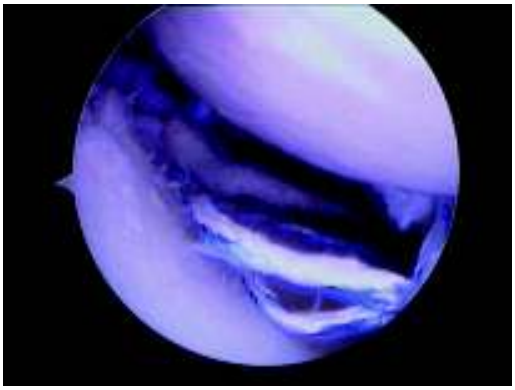

Fig. 19.17 The first horizontal suture (all inside) should join the remnant posterior horn to the Actifit™

released close to the meniscal bed. A blunt obturator or a probe may facilitate correct placement (Fig. 19.16a, b).

The fixation of the scaffold may be done with all inside sutures or with the inside-out or outside-in technique, depending on the site of the lesion and the personal experience of the surgeon. The first suture should begin from the most posterior part, joining the Actifit™ to the native meniscus tissue with a horizontal suture (not too tight, since it may cut the scaffold's structure and/or modify its position) (Fig. 19.17). A second horizontal suture should fix the anterior part of the Actifit™ to the anterior native tissue (Fig. 19.18a, b), followed by nonabsorbable vertical sutures, where possible, along the body of the scaffold. In the lateral meniscus a suture through the popliteus muscle is not detrimental. The stability of the Actifit™, once fixed, is tested with a probe and, subsequently, through the ROM of the knee (Fig. 19.19).

Rehabilitation

A specially designed rehabilitation protocol is available as booklet in the Actifit™ kit and published elsewhere [31, 32]. This rehabilitation protocol should be strictly followed, since it provides conditions, felt by the manufacturer, to be optimal for healing and protection of newly regenerated tissue.

In brief, no weight-bearing for 3 weeks, partial weight-bearing from the fourth week onward with gradual increase in loading during the following weeks. The total rehabilitation program will take 16–24 weeks. Resumption of sports can begin at 6 months after orthopedic consultation, and contact sports should not be resumed before 9 months after surgery.

Clinical Experience

Before Actifit™ was released widely, a prospective, multicenter proof-of-principle study was conducted in nine centers in Europe. The goal of the study was to assess the tissue ingrowth at 3 and 12 months after index surgery and the safety

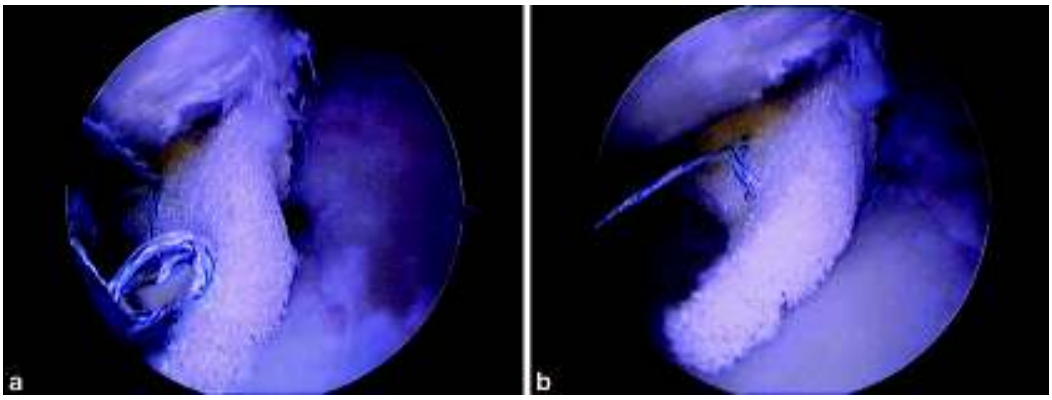

Fig. 19.18 **a**, **b** Sequence of horizontal suture for fixation of the anterior part of the Actifit^{TM} to the anterior native tissue

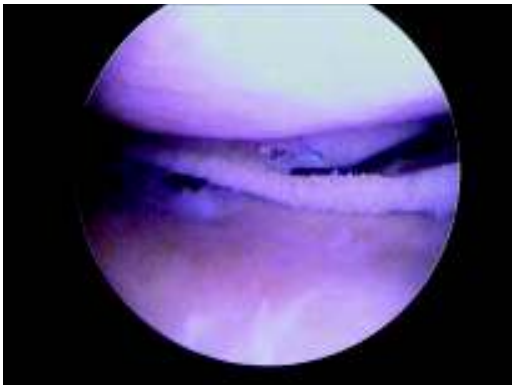

Fig. 19.19 Final vision of the Actifit^{TM} after fixation: The stability is tested with a probe

of the scaffold [27]. Efficacy (clinical outcomes-perceived pain, functionality, and quality of life) was assessed at 3, 6, 12, and 24 months after index surgery [33]. Details of results are well described in the above mentioned papers.

Key points of these studies are:

- Early tissue ingrowth into the scaffold at 3 months
- Biocompatibility of the scaffold and meniscus-like tissue found at biopsy at 12 months
- Clinically and statistically significant improvements in all clinical outcomes scores at 24 months, demonstrating improvement in both pain and function
- Stable or improved ICRS grades observed in 92.5 % at 24 months.

In the author's department, Actifit^{TM} scaffold implantation was started in 2010. Since then, 28 patients with an average age of 40 years and 8 months (16–55 years) have been treated. The mean follow-up was 11 months (6–20 months). Among 26 male and 2 female patients, 4 patients received a lateral meniscus implant, and 24 a medial. The implantation of Actifit^{TM} was associated with a valgus osteotomy (HTO) in four cases and with supracondylar femoral varus osteotomy (Distal Femoral Osteotomy) in one case. In 4 patients, an ACL reconstruction with hamstring tendons was performed.

Following Actifit^{TM}, good to excellent results were achieved in nearly 80 % of the cases. The IKDC showed 10 patients in group A, 13 in group B, and 5 in group C. Applying the Lysholm score, 10 patients had excellent results.

All patients experienced a substantial decrease in pain, as well as improved function and quality of life. Implantation of this meniscal scaffold combined with ACL reconstruction or a correction of a limb malalignment achieved better results. Worse results were associated with degenerative changes of the involved compartment (>3° of ICRS), or with uncorrected axial deviation (5–8°).

These results, despite a very short follow-up period, are in agreement with a trend toward improvements in all clinical outcomes scores, described in the multicenter prospective study published by Verdonk et al. [27].

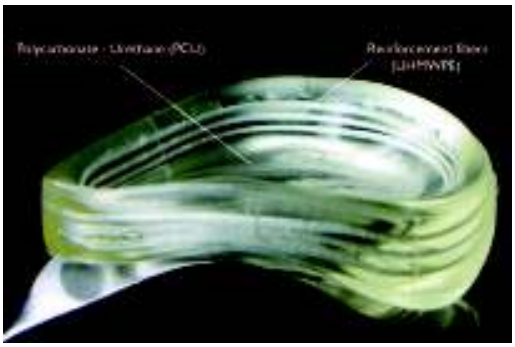

Fig. 19.20 The NUsurface®: a medial meniscus implant made of polycarbonate-urethane (PCU), reinforced circumferentially with ultrahigh molecular weight polyethylene (UHMWPE) fibers (Dyneema® Purity, DSM)

Interpositional Arthroplasty: NUsurface®

Background

A nonfixed, self-centered, medial meniscus implant (NUsurface®, Fig. 19.20) has been developed as a bridge treatment for middle-aged patients [34], suffering from joint pain associated with loss of meniscal function. The concept of a medial meniscus implant with a reliable biomechanical performance differs from the above two products as it does not rely on regeneration.

Geometry and Material The concept of a nonanchored device allows a simple implantation through a miniarthrotomy without damaging bone, cartilage, or ligaments, thus leaving all successive treatment options open. The implant was designed as a composite construct made of PCU, reinforced circumferentially with ultrahigh molecular weight polyethylene (UHMWPE) fibers (Dyneema® Purity, DSM), embedded during the manufacturing process to reproduce the structural characteristics of the natural meniscus, which consists of a solid matrix embedded with a highly orientated collagen fiber network [35]. The pliable matrix material is distributing articular pressure by permitting local material deformation, whereas the reinforcement is designed to restrain matrix flow and bear a high portion of the stresses. PCU is considered a durable material with high resistance to long-term wear, as published in several previous publications [36–42].

A representative geometric design for the meniscus shape was formed, based on the analysis of more than 130 human knee MRI-scans [43]. The lateral aspect of the implant body was designed to form a full discoid shape by creating an artificial "bridge" along the gap between the original medial insertion points of the meniscus (the region of the intercondylar notch). The preservation of the cruciate ligaments and prevention of undesired impingement were taken into account in the design, as well as knee alignment and stability.

Seven sizes are available that should be applicable for ~95 % of the population [44]. The volumetric difference between sizes is ~4 %.

Biomechanical Testing Biomechanical optimization of the material properties, as well as the functionality of the implant, was based on static and dynamic measurements in vitro in cadaver knees, fatigue tests, and finite element (FE) analyses.

Static In vitro Measurements The biomechanical evaluation of the implant included more than 1,500 in vitro compression tests in more than 30 cadaveric knees, assessing the implant's ability to distribute load on the tibial plateau. The compression test protocol is described in detail elsewhere [45]. In brief, the implants were inserted into the medial compartment of cadaveric knees, and were loaded under medial compression similar to the physiological load during gait. Pressure distribution under the implant was measured utilizing flexible sensors (Tekscan Inc., Boston, MA) and compared to those attained for the natural meniscus prior to meniscectomy (Fig. 19.21a). Contact pressure distributions measured on the tibial plateau were in very good agreement with those measured under the intact natural meniscus of the specific knee (Fig. 19.21b). Calculation of Peak-to-Average pressure relation (PAR) (3.1 ± 0.3) and contact area (658 ± 135 mm^2) for the implant were statistically indistinguishable when compared to PAR (2.7 ± 0.5) and contact

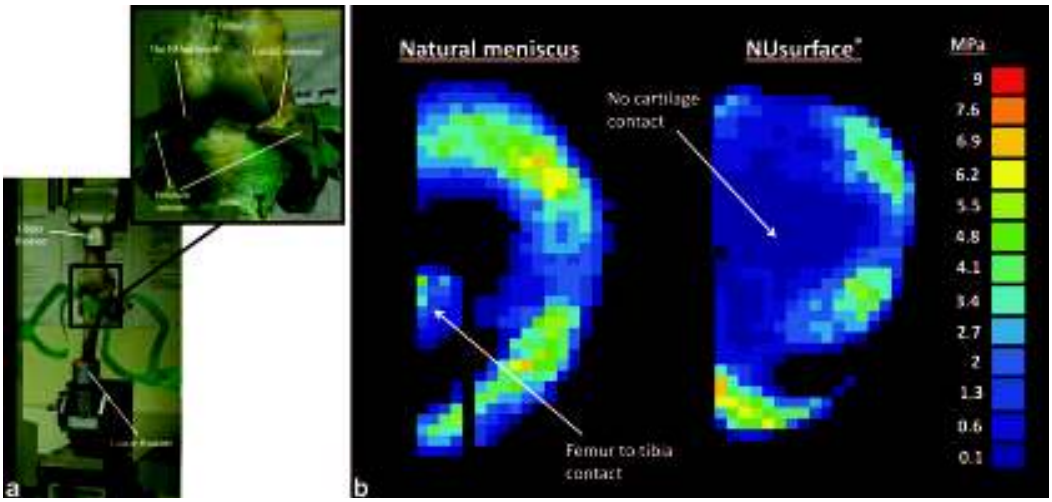

Fig. 19.21 **a** Pressure distribution under the implant measured with flexible sensors (Tekscan Inc., Boston, MA). **b** Contact pressure distributions on the tibial plateau were in very good agreement with those measured under the intact natural meniscus of the specific knee

area (642 ± 96 mm^2) measured for the natural meniscus ($p \geq 0.05$).

Dynamic In vitro Measurements In order to evaluate the stability of the implant under different kinematic conditions, a cadaver-based, robotic knee dynamic simulator was used (Cleveland Clinics, OH) [42]. Six cadaveric knees were prescreened prior to simulation by MRI and X-ray for sizing, and to assure ligament integrity and no clinical abnormalities. The knees were preassigned randomly to display combinations of normal and increased laxity following an MCL release, and 3° of posterior horn removal (normal, excessive, and total). Each specimen was fixed to 6° of freedom force/torque sensor and placed on a robotic manipulator (Rotopod R2000, Parallel Robotics System, Hampton, NH) in a way that retained as much soft tissue as possible. Motion and loading conditions were simulated dynamically by replicating the loads and knee flexion motion. Following, each knee was placed under physiologic joint loading with three repetitions of implant sizes (normal, undersized, and oversized).

In general, the nonanchored NUsurface® implant was found to be stable in the joint. Implantation of an undersized implant, and the presence of an ACL tear, however, increased the risk for subluxation/dislocation. Conversely, there were no subluxation or dislocation episodes when the implant was optimized or upsized in patients with complete removal of the posterior root.

Fifteen-Million Cycles Fatigue Test Cyclic mechanical compression/compression loading was applied to the implant according to fatigue tests requirements (ISO14243). MRI-based UHMWPE replicas of tibia and femur were used as compression surfaces. Fifteen-million loading cycles were applied on each specimen, and the implant's structure and functionality were examined before and after the tests. These tests demonstrated that the implant's components, PCU and UHMWPE fibers, were not affected in the long-term in respect to form, fiber-matrix bonding, and structure–function relationship. No significant dimensional changes were observed during the course of the tests, and pressure distributions post 15-milion loading cycles remained similar to those measured prior to the tests.

Finite Element Analysis An FE model of the medial knee with the PCU implant inside was developed and internal strains/stresses developed in the PCU bulk and the UHMWPE fibers were

calculated [46]. The model geometry was based on MRI-scans of a cadaveric specimen and analyzed under 1,200 N compression: comparable to the biomechanical evaluation and other published FE models. The model was validated by comparing computational results to analogous tibial plateau contact pressures, measured in cadaveric knees in vitro [45]. Peak stresses in the PCU were all lower than the maximal allowed stress (15 MPa). Similarly, the peak tensile stress calculated in the fibers was significantly lower than the material's yield stress (3.1 GPa).

Pre- and Intraoperative Sizing Validation: Cadaver Study The current surgical technique is based on cadaver studies, in which the specific surgical steps were tested. The goals of the study were to standardize the surgical procedure, and to validate the pre- and intraoperative sizing procedure.

Eight cadaveric knees (male = 2, female = 6, 50–90 years' old) had X-ray (AP and lateral) and MRI scans before the experiment, and preoperative size selection was conducted using both MRI and an X-ray template system [43]. The MRI sizing results were kept blinded from the surgeons participating in the lab, in order to validate the X-ray-based template system (Fig. 19.22). Implantation of trial implants was conducted starting from the smallest predicted size. Intraop size selection was based on both fluoroscopy, and arthroscopic evaluations, and was compared to MRI scans taken postimplantation.

The radio-opaque trial implants used in the cadaver study proved to be an excellent tool for evaluation of the implant movement in terms of anterior overhang and implant tracking during ROM. Also the X-ray templates proved to be simple to use, easier than MRI-based sizing. Based on this set of experiments, a sizing algorithm was developed to be used as part of the surgical technique (Fig. 19.23).

Animal Study The last preclinical stage was a sheep study in which an extensive postimplantation quantitative cartilage evaluation was conducted microscopically [47]. The material properties of the device were tailored to provide an optimal pressure distribution ability to reduce cartilage loads, and thus, relieve pain. Being able to conform moderately under load, without risking its integrity, is another important feature of this concept, which distinguishes it from other interpositional devices.

All procedures were approved by the Institutional Animal Care and Use Committee of the Technion University, Israel (#10-6-11-06) and are described in detail elsewhere [47]. Six ewes (1–2 years, 60–80 kg) were allocated for this study. The sheep underwent a full meniscectomy of the medial meniscus of their left knee, and were implanted with a PCU meniscus substitute (Fig. 19.24a–c). Smaller joint tolerance in sheep required the release and reattachments of the MCL from the epicondyle to ease the insertion of the implant. Subsequent to the rehabilitation period, the sheep were relocated to a large pen and were allowed to ambulate freely. Functionality of the joint was assessed by measuring mobility and ROM. Animals were euthanized at 3 ($n = 3$) and 6 ($n = 3$) months. Cartilage and the surrounding soft tissues of both knees were assessed macroscopically and microscopically, using a semiquantitative histological analysis, based on a modified Mankin scale [48]. The contralateral knee served as control.

From gross inspection, the PCU implant remained well-secured throughout the experimental period and showed no visible signs of wear. Gross and microscopic examinations of the explanted PCU implant's surfaces did not reveal any changes in their structural or material properties. Histological analysis showed relatively mild degenerative changes in the articular cartilage that were dominated by a loss of proteoglycan content and cartilage structure. However, the total osteoarthritic score did not significantly differ between the control and operated knees, and there were no differences in the severity of degenerative changes between 3 and 6 months postsurgery (Figs. 19.25 and 19.26).

Indications

In light of our experience from a first-in-man series conducted in the author's hospital in Negrar

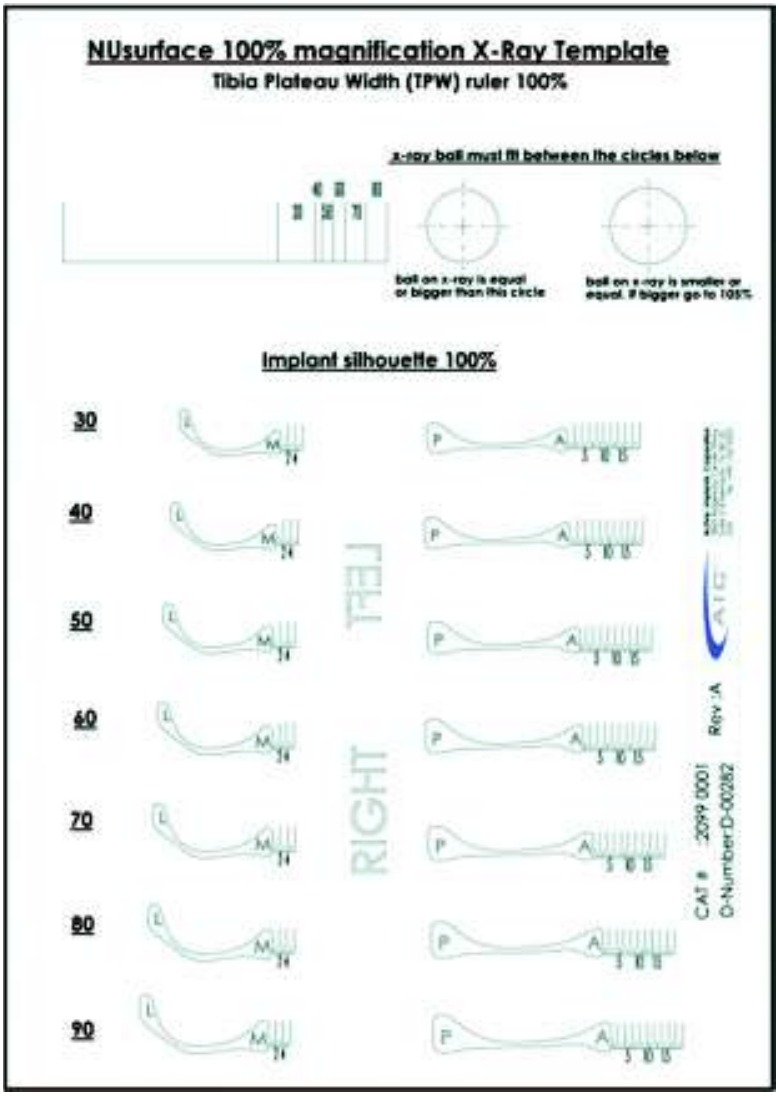

Fig. 19.22 X-ray template system validated during a blinded study on cadavers

(Verona, Italy, unpublished data), we have described inclusion and exclusion criteria for NUsurface® candidates, summarized in Table 19.1. These became the basis of a multicenter study, currently going on in Europe and Israel.

Surgical Technique

Arthroscopy The patient is placed in a supine position and the operative extremity is placed in a leg holder. The tourniquet is placed on the proximal third of the thigh. Standard anterolateral and anteromedial portals are established. Sometimes, a poster-medial portal can be used for managing the stability and the position of the device during flexion-extension in the posterior area. This portal is made with the knee flexed at 90°, with the aid of transillumination and a spinal needle approximately 2 cm above the joint line. A 5.5-mm cannula is left in this portal.

A joint inspection is accurately performed in order to confirm the integrity of the lateral and patellofemoral compartments, the cruciate ligaments, and the synovial tissue. An equally accu-

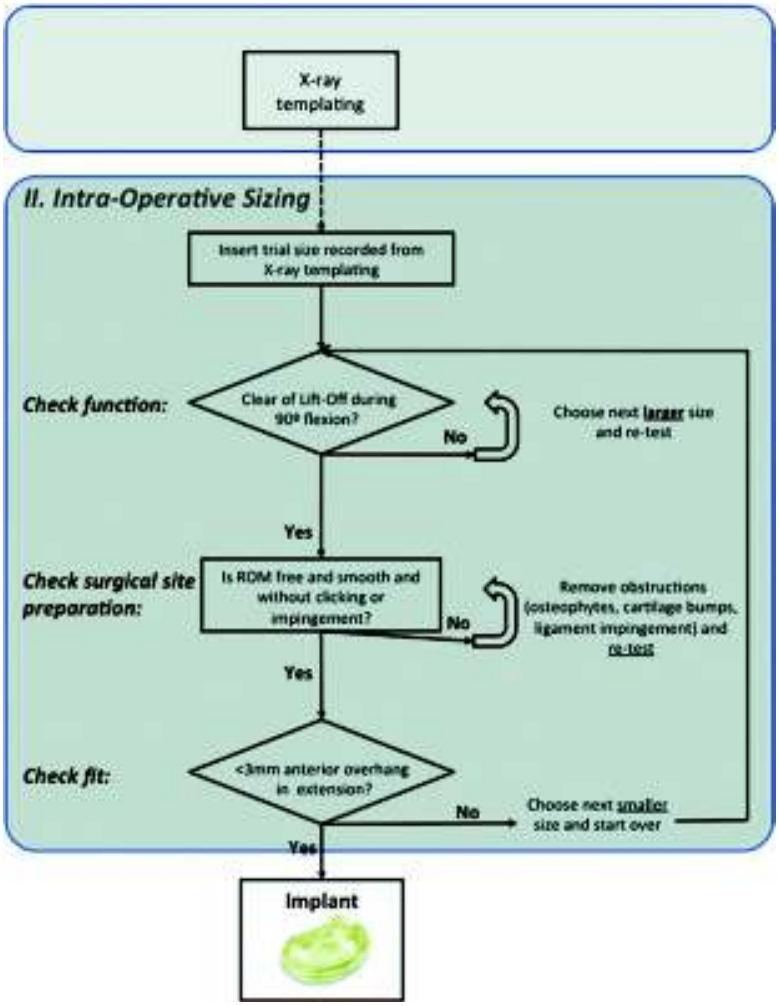

Fig. 19.23 Sizing algorithm developed during the cadaver study that may be used as part of the pre-op planning

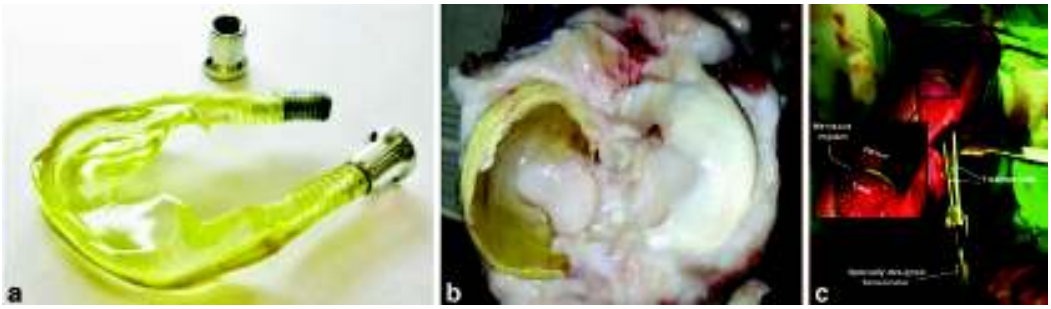

Fig. 19.24 Implantation system adapted to the sheep anatomy. **a** The implant. **b** Insertion after total meniscectomy and medial collateral ligament (MCL) detachment. **c** Fixation of the device to the tibia (surgical technique)

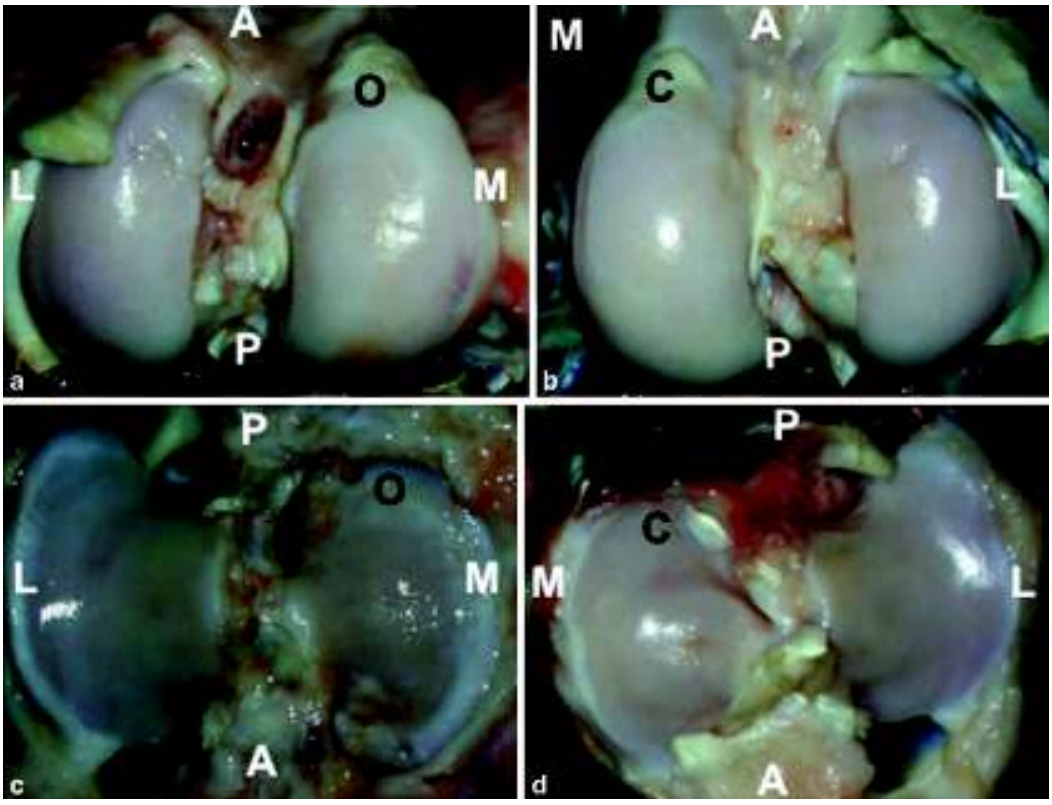

Fig. 19.25 Cartilage condition, 6 months postimplantation, as demonstrated in representative transverse images of the operated femur (**a**), control femur (**b**), operated tibia (**c**), and control tibia (**d**). Markings represent anterior (*A*), posterior (*P*), medial (*M*), and lateral (*L*) aspects, operated (*O*) and control (*C*) joints

rate inspection of the synovial tissue underneath the posterior cruciate ligament and the presence of osteophytes along the lateral contour of the medial femoral condyle are mandatory: in this area the lateral edge of the meniscus implant may impinge on such hypertrophic structures, causing malpositioning of the device.

The cartilage status in the medial compartment is inspected: grade IV lesions and femoral condyle deformity are absolute contraindications to NUsurface®. The articular cartilage treatment is a superficial debridement: to smooth the edges of the lesions to allow a free sliding of the device on the femoral condyle. A second check of the cartilage status must be performed with the definitive implant: during flexion-extension trials, it is possible to verify if the edges of the lesions may hamper the sliding path of the device and, in such a case, further edge smoothing has to be performed.

The inner part of the medial meniscus is removed completely using standard instrumentation and techniques. It is convenient to start from the posterior toward the anterior horn, always paying attention to leave the outer part of the circumferential fibers (about 3 mm) and the posterior root of the meniscus intact. The remnant tissue attached to the capsule should form an elastic border for the device, which should prevent eventual implant dislocations.

Open Surgery A longitudinal skin incision is made along the medial side of the patella with the knee flexed at 90°, approximately 5–7 cm long, starting from the apex of the patella down to the medial tibial metaphysis (Fig. 19.27). After the capsular incision, some synovial tissue and

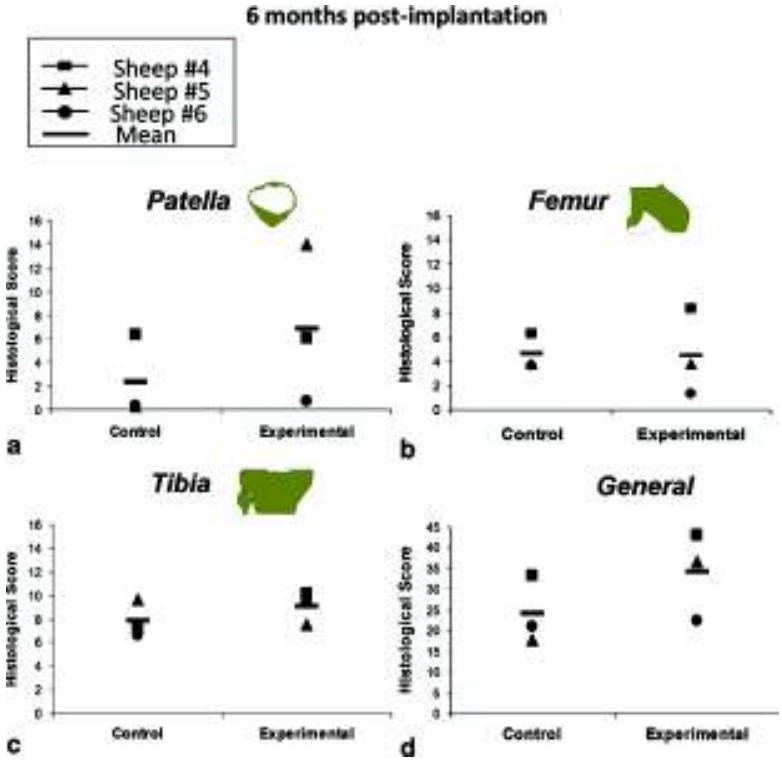

Fig. 19.26 Modified Mankin osteoarthritis scores of control and implanted joints, 6 months postimplantation, calculated for the patella (**a**), femur (**b**), tibia (**c**), and total joint (**d**)

fat pad can be removed to improve visualization of the medial side of the joint from the capsule to the notch area. The anterior horn of the meniscus is removed at this stage of the surgery. If the intermeniscal ligament must be cut in order to create more room for the NUsurface® insertion, it will be sutured back at the end of the surgery.

NUsurface® Insertion Preoperatively, it is possible to determine the appropriate size of the implant using a template superimposed on a standardized X-ray of the knee, which measures the dimension of the medial compartment in the anteroposterior and medial–lateral directions. Seven implant sizes are available from size 30–90. Each step in size represents an increase of ~4 % in all dimensions.

For each implant size a trial device of the same dimension, but with a circumferential radio-opaque line for intraoperative fluoroscopic positioning control is available (Fig. 19.28).

The optimal position for the device insertion is around 30° of knee flexion in valgus stress. The device is clamped by a dedicated inserter (Fig. 19.29) that holds it along the anterior border. After the NUsurface® is placed into the medial compartment, several cyclic flexion-extension movements are performed to center the device. The inspection should focus on medial side overhang; a few millimeters of medial extrusion are well tolerated by the medial capsular-ligament structures (Fig. 19.30). Avoiding lateral impingement in the notch area is another key point to allow good sliding movement (Fig. 19.31). The NUsurface® trial position can easily be controlled by fluoroscopy: this allows not only to confirm the static position, but also the displacement in flexion and extension, and to compare different sizes. The posteromedial portal allows visualization of the implant statically. Dynamically, this is technically demanding or sometimes impossible, since in flexion the posterior space narrows and the arthroscope may be pushed outside the capsule.

Table 19.1 Inclusion and exclusion criteria for potential NUsurface® patients

Inclusion criteria	Exclusion criteria
Have a degenerative and/or torn medial meniscus and/or previous meniscectomy confirmed by diagnostic MRI	Have evidence of a grade IV articular cartilage loss on the medial tibial plateau or femoral condyle that could contact the NUsurface® implant
Have a pain score of 75 or less on the KOOS pain scale, with 100 being normal	Have lateral compartment pain with lateral articular cartilage damage greater than grade II (OB), and/or lateral meniscus tear(s)
Be in neutral alignment ± 5° of the mechanical axis	Have a varus or valgus knee deformity > 5 degrees
Be between the age of 35 and 75 years at the time of the planned surgery	Have a laxity level of more than II according to the ICRS score, secondary to previous injury of the ACL, and/or PCL, and/or LCL, and/or MCL
	Have patella instability or nonanatomically positioned patella
	Have patellar compartment pain and/or patellar articular cartilage damage greater than Grade II OB
	Need a tibial osteotomy at the time of surgery
	Have an ACL reconstruction performed < 9 months before implanting the NUsurface® device
	Have any type of previously implanted prosthetic meniscus or ligament or knee implant made of plastic
	Have a knee flexion contracture > 10°
	Be unable to flex the knee to 90°
	Have a leg length discrepancy causing a noticeable limp
	Have had a previous major knee condyle surgery
	Have any type of knee joint inflammatory disease including Sjogren's syndrome
	Be morbidly obese with a BMI > 35

ACL anterior cruciate ligament, *BMI* body mass index, *ICRS* International Cartilage Repair Society, *KOOS* knee injury and osteoarthritis outcome score, *LCL* lateral collateral ligament, *MCL* medial collateral ligament, *MRI* magnetic resonance imaging, *OB* outer bridge, *PCL* posterior cruciate ligament

The insertion of the definitive implant is performed using the same technique described earlier.

Capsular closure is performed in the standard fashion, while evaluating for possible anterior impingement in full extension. A drain may be used for the first night.

Rehabilitation

The knee is placed in a cast in full extension for the first week. From the first day post-op, partial weight-bearing and quadriceps isometric exercises are allowed. Full weight-bearing as tolerated, hydrotherapy, and exercises in closed kinetic chain are started in the second week. Open kinetic chain exercises are allowed after 6 weeks. Proprioceptive exercises are encouraged, since lack of proprioception seems to be one of the main complaints of the patients during the first 2–3 months, post-op.

Clinical Experience

A first-in-man series has been conducted in the author's department starting in May 2008. Inclusion criteria were those mentioned in Table 19.1, but were extended to grade 4 cartilage degenerative disease according to Outerbridge Classification. The second major difference versus the mentioned inclusion criteria was that, no attention had been directed to the posterior root status of the involved meniscus. These two differences were mainly responsible for most of the failures

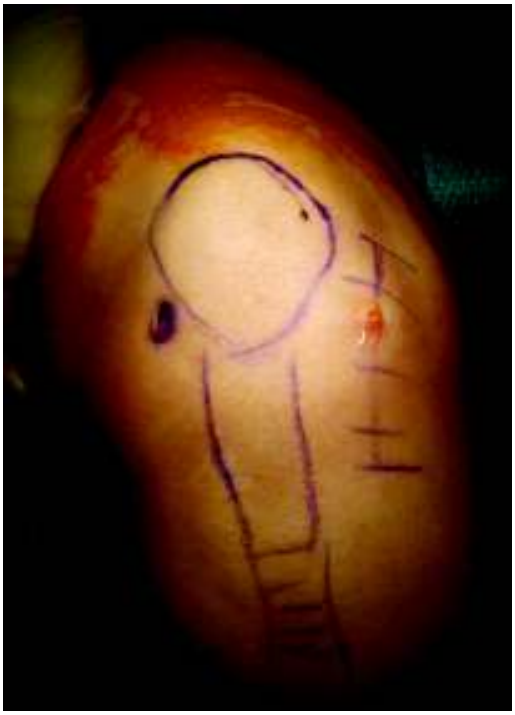

Fig. 19.27 The skin incision is made on the medial side of the patella, approximately 5 to 7 cm long

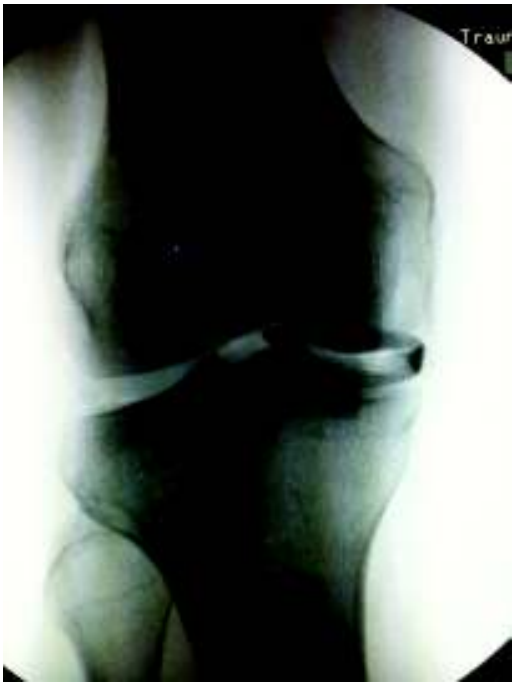

Fig. 19.28 Intraoperative fluoroscopic anteroposterior view of the trial

and implant dislocations (unpublished data). Based on this data, in March 2012 a prospective, multicenter, nonrandomized, open label study was started in Europe and Israel (seven centers).

Thus far, in our personal series (10 patients), no dislocation or other failure was observed. The current average follow-up (4, 5 months) is still too short to draw any significant conclusion. The results of all clinical outcome scores used (IKDC, KOOS, VAS, and EQ-5D) demonstrate an apparent trend toward an improvement within a selected population over 50 years of age, with medial pain and impaired functionality due to medial meniscus insufficiency.

Conclusions

Meniscus replacement still represents an unresolved problem in orthopedics. Meniscal allografts have been shown to heal to the capsule and relieve pain [49]. However, in addition to problems related to availability, size matching, cost, and risk of disease transmission, allograft menisci undergo remodeling after implantation, causing shrinkage and reduced mechanical strength [50, 51]. These factors may lead to tearing of the allograft and contribute to an uneven distribution of load, instability, and recurrence of degenerative damage.

Meniscal substitutes based on synthetic or natural polymers have been described [30, 52–54]. Most of these prostheses are based on biodegradable materials, which form temporary scaffolds that degrade in the body over time and are replaced gradually by newly formed tissue. Potential shortcomings of this approach include the lack of durability, associated with most biodegradable materials under in vivo knee loading conditions [52, 55], as well as the variability in the individual patient's biological response to the implant, limited age of the target population, and the quality of the tissue formed.

Currently, conservative care (e.g., knee bracing, activity modification, and injections), and even primary, secondary, or multiple menisectomies, represent the mainstream treatment

Fig. 19.29 Dedicated instruments to insert and to pull out the NUsurface®

for a ±50-year-old patient with symptoms from meniscal functional deficiency. At a later age, e.g., older than 65 years, clinicians often choose arthroplasty. Traditional unicompartmental knee arthroplasty (UKA) is regaining popularity, but requires significant bone resection and subsequent modification of the patient's activity. Total knee arthroplasty (TKA) is a reliable procedure, but it is not usually recommended for younger patients, less than 55 years of age, who might require subsequent revision surgery.

The treatment gap noted above may now have treatment options which are in the investigational stage. Further research and development may eventually extend these biological options to more challenging meniscal lesions, in order to truly regenerate meniscal tissue with biological and biomechanical properties close to native meniscus.

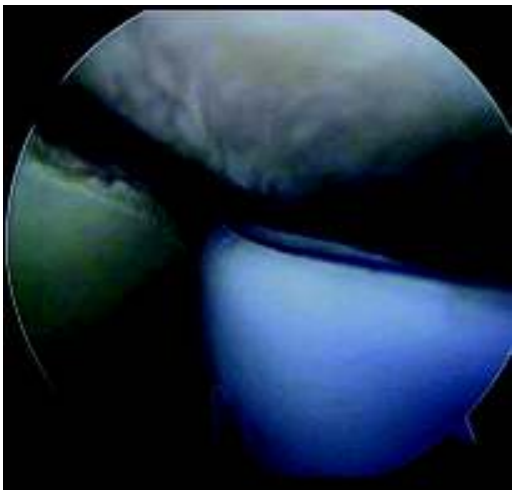

Fig. 19.30 The size of the trial fits perfectly between the femur, the tibia, and the remnant meniscus

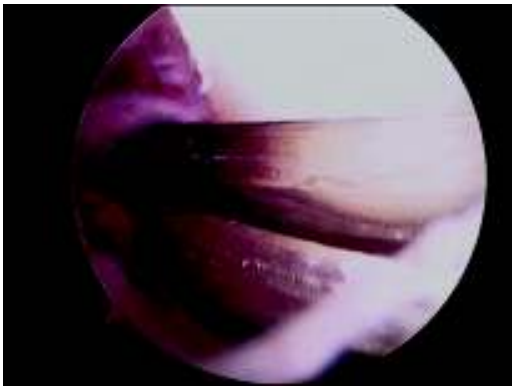

Fig. 19.31 No impingement of the NUsurface® underneath the PCL

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