NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of partial replacement of the meniscus of the knee using a biodegradable scaffold

Using keyhole surgery to repair damaged knee cartilage with a biodegradable implant

The meniscus is a crescent-shaped cartilage inside either side of the knee. It acts as a shock absorber between the long bones of the leg. It can be damaged by injury or overuse, causing pain, swelling and locking of the knee. In this procedure, a biodegradable implant is placed into the meniscus by 'keyhole' knee surgery. The implant works as a scaffold to support re-growth and repair of the damaged meniscus. The aim of the procedure is to relieve pain and restore the mobility of the knee.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in November 2011 and updated in May 2012.

Procedure name

- Partial replacement of the meniscus of the knee using a biodegradable scaffold

Specialty societies

- British Orthopaedic Association
- British Association for Surgery of the Knee

Description

Indications and current treatment

The menisci are semi-lunar wedge-shaped fibrocartilaginous structures which act as shock absorbers, spreading the load on the articular surfaces of the knee.

The menisci can be damaged (often a tear) as a result of acute injury or degeneration which may cause pain and/or locking of the knee. It is believed that meniscal damage is associated with a higher risk of knee osteoarthritis in the longer term.

Minor meniscal damage can be treated conservatively (including by rest and physical therapies). For more severe cases, treatment usually involves removal of the damaged part of the meniscus (partial meniscectomy).

Meniscal repair is possible only in a minority of patients. This depends on the proximity of the damage to the peripheral vascular region of the meniscus (where good blood supply allows meniscal healing), the pattern of the damage and whether there is damage to other knee joint structures.

Implantation of a scaffold for partial replacement of the meniscus of the knee aims to support the body's own physiological pathways for healing by providing a 3-dimensional matrix for cell adhesion and vascular ingrowth, when attached to the vascular portion of the meniscus. In the short term the procedure aims to restore the load-bearing and shock-absorbing functions of the damaged meniscus, contributing to pain relief and restoring functional mobility. In the long term it aims to reduce the risk of osteoarthritis and the need for further operations. A strict rehabilitation regime is usually employed after the procedure, which may include several weeks of restricted weight bearing and temporary bracing to limit knee movement.

The types of scaffolds available for this procedure include those made of synthetic polyurethane and implants made of collagen derived from animal sources.

What the procedure involves

Implantation of a biodegradable scaffold for partial replacement of the meniscus of the knee aims to support re-growth and repair of the damaged meniscus.

The procedure may be done with the patient under general or regional anaesthesia. Using an arthroscope, damaged sections of the meniscus are excised, leaving a residual meniscal rim in the vascular zone. The size of the defect is measured and the implant is trimmed to match it. The implant is then introduced into the joint via one of the portals and sutured to the remaining meniscal rim. This may require extra skin incisions to provide sufficient access.

Outcome measures

Lysholm knee scale:

- originally designed to assess ligament injuries of the knee
- outcome measure that contains 8 domains: limp, locking, pain, stair-climbing, support, instability, swelling, and squatting
- score of 0 to 100 is calculated:
  - 95 to 100 indicates an excellent result
  - 84 to 94 indicates a good result
  - 65 to 83 indicates a fair result
  - less than 65 indicates a poor result.

Tegner activity scale

The Tegner activity scale was designed as a score of activity level to complement other functional scores (for example, the Lysholm knee scale) for patients with ligamentous injuries. It is the most widely used activity scoring system for patients with knee disorders. Scores range from 0 (indicating the highest degree of disability relating to the knee joint) to 10 (indicating ability to participate in competitive sports).

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to partial replacement of the meniscus of the knee using a biodegradable scaffold. Searches were conducted of the following databases, covering the period from their commencement to March 2012: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. Language and date of publication restrictions were applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with partial meniscus loss or damage.
Intervention/test	Implantation of a biodegradable scaffold.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 600 patients from 2 randomised controlled trials (RCTs)[1,2], 1 non-randomised study[3] and 5 case series[4–8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on partial replacement of the meniscus of the knee using a biodegradable scaffold

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details

Rodkey, WG (2008)[1]

Randomised controlled trial

USA

Recruitment period: not reported

Study population: Patients with irreparable injury to or previous partial loss of one medial meniscus with an intact rim. Patients with no prior surgery on the involved meniscus were designated as the 'acute' arm and those with prior surgery on the involved meniscus were designated as the ''chronic' arm

n=**311**

Acute arm: n=157 (75 implants vs 82 control)

Chronic arm: n=154(85 implants vs 69 control)

Patients randomised to the control arms underwent an appropriate PM and joint debridement (if indicated).

Age: acute arm: mean 40 years; chronic arm: mean 38.5 years

Sex: acute arm: 85% male; chronic arm: 72% male

Patient selection criteria: Patients 18-60 years of age who had an irreparable injury to or previous partial loss of one medial meniscus, with an intact rim. Involved knees had to be in neutral alignment with weight-bearing axis. Patients with a full-thickness

Key efficacy findings

Number of patients analysed: **308**

Acute arm: 157 (75 vs 82) ; chronic arm: 151(82 vs 69)

Functional activity: Lysholm functional score.

	Acute		Chronic	
	Implant	Control	Implant	Control
Mean change from pre-operative score	26	28	16	22
Mean score at last follow-up	90	87	79	78

Study reported that the mean Lysholm scores were not significantly different between the two groups. P-values not reported.

Pain

	Acute		Chronic	
	Implant	Control	Implant	Control
Mean change from pre-operative score	16	21	18	18
Mean score at last follow-up	5	6	19	21

Reported that pain was assessed during rest, ADL and at highest levels of activity. Study reported mean pain scores were not significantly different between the two groups. P-values not reported.

Activity (at 5 year follow-up)

Key safety findings

Serious or clinically relevant complications (as classified by surgeon-investigator and requiring some treatment) in the study knee were reported in 7.6% (12/157) and 7.3% (11/151) in the implant and control groups, respectively.

	Implant	Control
Pain	2	7
Swelling/ effusion/ redness	4	1
Instability	1	0
Nerve injury/ numbness	1	1
Infection/ fever	1	1
Deep vein thrombosis	1	1
Wound-related/other	1	0
Patello-femoral symptoms	1	0

Of the 12 documented serious complications in patients with implants, 7 were classified as probably or at least possibly related to the implant. A skin infection developed at a portal site at 1 week and penetrated into the joint (not directly related to the implant). The implant was removed. Further details on the other complications not reported.

Comments

Follow-up issues:

- Acute arm: All patients followed-up; chronic arm: 98% followed-up
- Reasons for loss to follow-up in the 'chronic' study arm (n = 3) were death (n = 2) and an early infection (n = 1)
- For time-to-event analysis, data were censored for patients for whom follow-up had not been completed.

Study design issues:

- Patients were randomised and analysed separately for the 'acute' arm and the 'chronic' arm.
- Patients randomised to the two intervention arms were required by protocol to have a second-look arthroscopy and biopsy 1-year after the placement.
- The control group was not required to undergo a planned second-look arthroscopy.
- A-priori sample size calculation was carried out. With 80% power, at p = 0.05, 128 patients were needed for each study arm. A 20% drop-out rate was accounted for and it was determined that a minimum of 154 patients was needed to be enrolled in each study arm.
- Sequence generation was

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details

chondral lesion, posterior cruciate ligament insufficiency, concurrent pathological involvement of the lateral meniscus requiring excision >25% were excluded.

Technique: Partial replacement of the meniscus performed arthroscopically with an implant (CMI [ReGen Biologics]). Implant was trimmed to the appropriate size to fill the meniscus defect measured with the use of specific instrumentation. After delivery of the implant into the join, it was sutured to the remnant meniscus with non-absorbable sutures using an inside-out technique.

Follow-up: **mean: 59 months**

Conflict of interest/source of funding: Funding or grants received by one or more of the authors from ReGen Biologics.

Key efficacy findings

Assessed using Tegner index

Acute arm: Both the implant and control group regained an average of 41% of their lost activity.

Chronic arm: Lost activity level regained was 42% vs 29% for the implant and control groups, respectively (p = 0.02).

Patient satisfaction (with the current condition of their knee)

	Acute		p	Chronic		p
	Implant	Control		Implant	Control	
Very/ somewhat satisfied	82%	75 %	>0.05 (not significant)	66%	49 %	0.09

Absolute numbers not reported.

Patient self-assessment score

	Acute		Chronic	
	Implant	Control	Implant	Control
Mean change from preop score	0.9	1.1	0.7	0.9
Mean score at last follow-up	1.6	1.6	1.9	2.1

Details on scale used to assess this outcome not reported

Reoperations(defined as an additional surgical procedure on the study knee, outside the protocol, as a result of disabling or persistent pain and/or mechanical symptoms that could possibly involve the meniscus).

Reoperation rate was 9.5% and 22.7% in the implant and control groups, respectively.

Primary presenting symptom for reoperations:

	Acute	Chronic

Key safety findings

Inflammation of synovium

Observed in < 5% of the cases in biopsy specimens of the implant. None of these cases were associated with any clinical findings of synovitis at second-look arthroscopy.

Comments

computer-generated and concealment of allocation was undertaken using sealed envelopes at a centralised location. An ITT analysis was carried out. Patients and personnel were not blinded. Blinding of outcome assessors unclear for all except histological evaluations, which were done independently.

- Time-to-event analysis (reoperation at 5 years) was undertaken using the Kaplan-Meier method. Paired t-test for pre- and post-operative comparisons for continuous variables.
- Validated methods used for assessing outcome measures for functional assessment and pain. Lysholm functional score: rated on a scale of 0 to 100, where a higher score indicates knee pain has not affected ability to manage in everyday life. Pain measured using VAS, with scores ranging from 0 (indicating no pain) to 100 (indicating worst possible pain).
- Activity level assessed using Tegner index – authors defined this outcome as a percentage of lost activity level that was regained as result of treatment; An index of 1.0 indicated the patient regained all (100%) of the of

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments

	Implant n=75	Control n=82	Implant n=82	Control n=69
Pain	2	4	5	11
Swelling/ effusion	1	0	2	1
Stiffness/ decreased motion	1	0	0	0
Locking/ catching/ popping	0	0	1	2
Instability	1	1	0	1

The risk of a reoperation at 5 years in patients who had PM only: OR=2.7 (95% CI 1.2 to 6.7). p=0.04

Survival rate at 5 years

Survival rate (with reoperation as the end-point) 89% vs 74% for the implant vs control groups, respectively.

Technical efficacy

No failures caused by a lack of healing of the implant to the meniscus rim or gross tearing of the implant were observed.

Explantation of the implant was performed in 1 patient in the acute group (explanted early because of mechanical failure) and in 2 patients in the chronic group (causes not stated).

Increase in meniscal tissue

	Acute		Chronic	
	Implant n=65	Control	Implant n=76	Control
Percent defect filled	54±28	0*	58 ± 27	0*

*Zero value was assumed on the basis of values for historical

the activity level compared with recalled activity level pre-injury. Unclear if this is a validated method.

Study population issues:

- Baseline characteristics reported no significant differences between the treatment groups for age and sex within the study arms (reported p > 0.05). Baseline scores for pain, functional or activity levels not reported.
- Study reported no significant differences between the treatment groups within the study arms on the number of concurrent ACL reconstructs. (reported p > 0.05).

Other issues:

- Study reported groups were randomised and analysed separately but not the case for all outcomes. Pooled results reported for safety outcomes.
- Patients randomised to the implant received a different rehabilitation protocol to the control (PM alone) groups.
- The surgeon-investigator at each site solely determined the severity of each complication and whether it was related to the implant.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments

controls. Significant difference ($p<0.05$) between the treatment groups within the study arms. Data expressed as mean ±SD

Second-look arthroscopy in 88% (141/160) patients at 1-year showed the implant had resulted in a significant (p=0.001) increase in total tissue surface area, appeared grossly meniscus-like and well integrated with the host meniscus rim.

Joint cartilage breakdown

Outerbridge score

	Acute		Chronic	
	Implant n=75	Control n=82	Implant n=82	Control n=69
At index surgery	1.3	1.2	1.5	1.7
At 1-year arthroscopy follow-up	1.6	-*	1.9	-*

*Results for patients in the control group not reported because these patients did not undergo second-look arthroscopy.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments
Linke RD (2006)[2] **Randomised controlled trial** Country: not reported Recruitment period: January 2001 to May 2004 Study population: Patients with subtotal loss of medial meniscus and varus morphotype n=**60 (30 HTO plus implant vs 30 HTO only)** Age: range: 19–68 years Sex: not reported Patient selection criteria: Indications: traumatic or degenerative loss of a large part of the medial meniscus in the presence of intact anterior and posterior meniscus insertions and an intact outer rim, subtotal loss of the medial meniscus in a biologically young patient with high activity levels, body mass index <25 kg/m^2. Contraindications include: complete loss of medial meniscus, untreated knee ligament stability, untreated varus deformity with an axial deformity of >5^o, infection of the joint, ≥grade IV chondral defect, bovine allergy, obesity. Technique: Through standard anterior arthroscopy portals diagnostic arthroscopy was undertaken. The medial meniscus was resected and the implant (CMI) was fixed with non-resorbable sutures using an inside-out technique. All patients underwent HTO. Follow-up: **24 months** Conflict of interest/source of funding:	Number of patients analysed: **39 (23 vs 16)** **Functional activity** Lysholm scores: IKDC: **Pain** **Evaluation of implant** Implant completely healed in 34.8% (8/23) and partially healed in 30.4% (7/23).In 30.4% (7/23) patients there were poor results with only small remains of the implant left.	**Dislocation of implant** The implant underwent a 'disorganisation of its structure in the posterior part of the meniscus' and had to be explanted in 1 patient because of luxation. .	**Follow-up issues**: • 65% followed up. Study reported on arthroscopies 'evaluated so far 8–18 months post surgery'. **Study design issues**: • Patient recruitment method not reported. Details of sample size calculation, method of randomisation, concealment of allocation and blinding not reported. • Validated methods of assessment for functional assessments (Lysholm and subjective IKDC form). Lysholm score range: 0 to 100, where a higher score indicates knee pain has not affected ability to manage in everyday life. IKDC score range: 0 to 100, where a higher score is interpreted to mean no limitation with activities of daily living or sports activities and the absence of symptoms. • Pain measurements based on subjective assessment where 0 = no pain and X = intolerable pain [as reported in study] **Study population issues**: • Baseline comparability not reported. **Other issues**: • Postoperative management for all patients started from first postoperative day. Full

	HTO + implant	HTO only	p
Pre-operative	65.2	67	NR
At final follow-up	93.6	91	NR

	HTO + implant	HTO only	p
Pre-operative	65.2	67	NR
At final follow-up	93.6	91	NR

	HTO + implant	HTO only	p
Pre-operative	4.9	5.2	NR
At final follow-up	2.2	1.5	NR

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments
not reported			sporting activity after 6 months.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments
Zaffagnini S (2011)[3] **Non-randomised trial** Italy Recruitment period: October 1997 to March 2000 Study population: Patients with acute (had no prior surgery) or chronic (1,2or 3 surgical procedures) meniscal injuries self-selected to undergo partial replacement of the medial meniscus or PMM. n=**36 (18 vs 18)** Age: range : 24–60 years Sex: 100% males Patient selection criteria: Participants between 15–60 years of age with irreparable acute meniscal tears requiring PM or chronic prior loss of meniscal tissue >25%. Included patients had intact anterior and posterior attachments of the meniscus and intact rim (1 mm or greater) over the entire circumference of the involved meniscus with a contra-lateral healthy knee. Exclusion criteria included diagnosis of Outerbridge grade IV, documented allergy to collagen, history of rheumatoid arthritis, inflammatory arthritis or autoimmune diseases. Technique: Partial replacement of the meniscus with an implant (CMI, ReGenBiologics). The implant site was prepared to create a meniscus	Number of patients analysed:**33 (17 vs 16)** 		Implant	PMM	Reported p value
Pain	1.2 (0.9)	3.3 (1.8)	0.004
Lysholm functional	90*	80*	0.062
Tegner activity scale	75 (27.5)	50 (11.67)	0.026
IKDC	7A and 10B	4B and 12C	0.0001
SF-36 Physical Health Index	53.9 (4.0)	44.1 (9.2)	0.026
SF-36 Mental Health Index	54.7 (3.8)	43.8 (6.5)	0.004 | For parametric variables, results reported as mean (SD) and for non-parametric variables, expressed as median (IQR) * estimated from graph **Reoperation** 2 patients in each group required reoperation (arthroscopic debridement for swelling and HTO for other patients). Reasons were: swelling in 2 patients (1 in each group) and pain and swelling in 2 patients (1 for each group). Patients recovered without sequelae.	Swelling and pain in implant group (6%) was assumed to be related to the device. Timing of assessment was unclear. Patients were successfully treated by means of arthroscopic debridement and HTO. **'Myxoid degeneration'**(based on MRI evaluation) In 4 patients MRI evaluation showed a normal signal with reduced size and in 2 patients MRI evaluation revealed no recognisable implant.	**Follow-up issues**: • Passive follow-up. 92% followed-up. Reasons for loss to follow-up were because of a tibial plateau fracture in 1 patient in the implant group and 2 patients refused to complete the evaluation in the PMM group. **Study design issues**: • Non-consecutive enrolment. Patients selected the treatment. • Self-selection may have led to more older patients choosing PMM (mean age: 44 years) while younger patients chose partial replacement of the meniscus (mean age: 38 years). • Blinding not possible for some outcomes as self-reported. Outcome assessors for MRI evaluations blinded. • Statistical tests used: Mann-Whitney for non-parametric variables (Lysholm, Tegner activity) and independent Student t-test for parametric ones (VAS; SF-36 scores) • Patients received physical therapy from the first postoperative day and the regimen differed between the implant and PMM group (except for those who underwent the microfracture

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments
defect without degenerative tissue. Extra blood supply was provided by holes punctured in the peripheral rim and the anterior and the posterior meniscal attachment points were trimmed to accept the scaffold. The dehydrated implant was trimmed to fill the defect and sutured with an in-out suturing technique, vertical stitches every 5 mm and horizontal stitches in the posterior and anterior junctions. All surgery was performed by the same experienced senior surgeon. For arthroscopic PMM, 'a standard approach' was used (no further details provided). Follow-up: **mean : 133 months** Conflict of interest/source of funding: Study reported no conflicts of interest in authorship and publication.			procedure, who followed the same rehabilitation programme as the MCMI group). All patients followed a rehabilitation protocol for 6 months until they returned to full unrestricted activity. • Validated methods of outcome assessment reported. VAS for knee pain assessed during rest and activity; measured on a scale from 0 (indicating no pain) to10 (worst possible pain); Lysholm score range from 0 to 100, where a higher score indicates a better outcome. QoL was assessed with a self-administered SF-36 questionnaire. Objective IKDC form on seven domains (effusion, passive motion deficit, ligament examination, compartment findings, harvest site pathology, X-ray findings and functional test) with each domain graded: A: normal; B: near normal; C: abnormal; D: severely abnormal. **Study population issues**: • Study reported that were no statistically significant differences between groups at baseline for age, sex and body mass index (p values not reported). No significant differences in number of ACL reconstructions at time of index surgery.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
			• During arthroscopy, grade III Outerbridge medial femoral condyle chondropathy diagnosed in 4 patients (2 in each group) and treated by the microfracture technique. **Other issues**: • Numerical values for preoperative scores not reported. These were illustrated on a graph. Study reported that the 'preoperative values were comparable' between the two groups. • Rehabilitation protocols were different between the groups, but all patients followed a programme for 6 months until they returned to full unrestricted activity.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments

Verdonk R (2012)[4]

Case series

9 centres in Europe

Recruitment period: March 2007 to April 2008

Study population: Patients with irreparable partial meniscal lesions.

n=**52 (34 medial and 18 lateral lesions)**

Age: Mean 30.8 years (SD 9.4)

Sex: 75% male

Patient selection criteria: Patients between the ages of 16 and 50 years with irreparable medial or lateral meniscal tear or partial meniscus loss with intact rim, with stable knee joint or knee joint stabilisation procedure within 12 weeks of index procedure and with International Cartilage Repair Society classification ≤2. Patients with more than 3 prior surgeries on the involved meniscus, BMI > 35, total meniscus loss or unstable segmental rim defect or multiple areas of partial meniscus loss were excluded.

Technique: All patients underwent arthroscopic PM with surgical debridement to the vascularised zone. Partial replacement of the meniscus was done using a polyurethane scaffold (Actifit®). The implant was cut to fit the void, placed into the knee joint through the anteromedial or anterolateral portal and sutured to the

Number of patients analysed: 52

Functional outcome scores (reported as mean [SD])

Scale	Baseline	24 months
VAS pain	45.7 (26.2)	20.3 (23.5)
IKDC	45.4(17.8)	70.1(23.0)
Lysholm	60.1 (19.2)	80.7 (19.5)
KOOS		
Symptoms	64.6 (22.3)	78.3 (18.5)
Pain	57.5(22.2)	78.6(22.5)
ADL	68.8(21.4)	84.2(21.2)
Sports	30.5(28.7)	59.0(33.4)
QoL	33.9 (19.3)	56.6(24.2)

Improvement from baseline was significant on all scales (p<0.0001)

Treatment failure

(defined as additional surgical procedure on the index defect. The need for an additional procedure was of unknown, possible, probable or definite relation to the scaffold and/or the index procedure)

Overall treatment failures: 17.3% (9/52)

	Reasons; n	Relationship to scaffold
Lateral meniscus 33% (6/18)		
<3 months after surgery	Arthroscopic removal of suture due to pain (n=1)	Not related to scaffold

Safety events

Reported in 17.3% (9/52) patients. All events were considered unrelated to the scaffold (unless otherwise indicated) and were reported to have resolved with treatment.

	Reasons; n
Lateral meniscus	
3–12 months after index surgery	Pain and swelling (treated with suture removal) (n=1)
12 months (during relook arthroscopy)	Debridement of non-integrated scaffold material (n=2) (unknown if this was related to scaffold)
	Meniscus allograft transplant (n=1)
24 months	A tear in tissue/scaffold construct (treated with an all-inside suture) (n=1)
Medial meniscus	
< 3 months after surgery	Postoperative infection (within 1 week)
3–12 months	Ongoing pain in patient with severe osteoarthritis(treated by unicompartmental knee arthroplasty)

Follow-up issues:

- 25% lost to follow-up for clinical outcomes data and 23% lost to follow-up for MRI data. Reason for loss to follow-up (where reported) was because of a serious adverse event (n=6) and patient unavailability unrelated to procedure (n=1).

Study design issues:

- Sample size of 50 patients calculated to enable a meniscal repair failure rate of 20% (95% CI 8.9% to 31.1%).
- Data from last observation carried forward in place of missing or non evaluable data.
- Study included treatment failures that occurred during the protocol-stipulated relook arthroscopy.
- A change of 10 mm on the VAS scale is considered a clinically significant change. A change in 10 points on the overall Lysholm score is considered clinically relevant. IKDC score rated on a scale of 0–100, with a higher score indicating better function. A change of 11.5 points indicates a clinically significant difference. KOOS score rated on a scale of 0–100, with a higher score

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings			Key safety findings		Comments
native meniscus. Follow-up: **2 years** Conflict of interest/source of funding: One author is an employee of Orteq Ltd, all authors or their departments received funding/sponsorship from Orteq Ltd and sponsor helped in preparing the first draft of the study.	3–12 months after index surgery	Arthroscopic removal of suture due to pain (n=1)	Unknown		Pre-existing osteochondritis dissecans (treated using mosaicplasty)	corresponding to better function. A change in a subscale score of >10 points is a clinically significant change. **Other issues**: • All patients were required to follow a rehabilitation protocol for 16 to 24 weeks. No weight bearing until week 4, to full weight bearing at week 9 and a gradual return to sports at 6 months after index surgery. • Technique for the procedure was reported in an interim report of the study (Verdonk 2011). This study is included in appendix A.
	12 months (during relook arthroscopy)	Debridement of non-integrated scaffold material (n=2)	Definitely related to scaffold	12 months (during relook arthroscopy)	Dislocated tissue/scaffold after uncontrolled twisting of the index knee (requiring removal of scaffold)	
		Tear in tissue/scaffold construct (treated with an all-inside suture) (n=1)	Definitely related to scaffold	24 months	Chondromalacia (repaired using microfracture).	
	24 months	Pain (n=1) requiring arthroscopy	Possibly related to scaffold			
	Medial meniscus 8.8% (3/34)					
	< 3 months after surgery	Postoperative infection (within 1 week after index surgery) (further information not reported)	Not related to scaffold			
	3–12 months after index surgery	Ongoing pain (treated by unicompartmental knee arthroplasty) to (n=1)	Not related to scaffold			
	12 months (during relook arthroscopy)	Dislocation of tissue/scaffold construct after uncontrolled twisting of the index knee (further information not reported)	Not related to scaffold			

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Zaffagnini S.(2009)[5]
Case series
(Study reported results for 2 case series studies)
Italy
Case series 1
Recruitment period: not reported
Study population:
Patients undergoing partial replacement of the medial meniscus.
n=30
Age: range 28–67 years
Sex: not reported
Patient selection criteria: not reported
Technique: Partial replacement of the medial meniscus with an implant (Medial CMI, ReGen). Patient was placed in a supine position with the knee at 90 degrees of flexion. Following preparation of the implant site, the anterior and the posterior attachment points were trimmed in a square shape to accept the scaffold. The dehydrated implant, in a sterile package, was measured, trimmed to fill the defect and inserted into the defect using a vascular clamp. The stability of the implant was tested with a probe.

Follow-up: mean 8.1 years
Conflict of interest/source of funding: not reported</td>
<td>Case series with patients undergoing partial replacement of the medial meniscus
Number of patients analysed:22
Functional activity
<table>
<tr><th></th><th>Pre-operative</th><th>Follow-up</th><th>p value</th></tr>
<tr><td>Lysholm score</td><td>NR</td><td>95.0 (8.7)</td><td>NR</td></tr>
<tr><td>Tegner activity</td><td>4.3 (2.3)</td><td>5.4 (1.6)</td><td>0.004</td></tr>
<tr><td>WOMAC</td><td>NR</td><td>96.4 (8.0)</td><td>NR</td></tr>
</table>
Data reported as mean (SD)
All patients were able to return to their usual daily life activities without any limitation in a mean time of 3 months after surgery.
Pain
<table>
<tr><th></th><th>Pre-operative</th><th>Follow-up*</th><th>p value</th></tr>
<tr><td>VAS</td><td>5.0 (0.9)</td><td>1.0 (1.12)</td><td><0.0001</td></tr>
</table>
*Absence of pain reported in 8 patients
Restriction in range of motion
Compared with the opposite leg, a flexion deficit of 10 degrees was observed in 13% (4/30) patients and a combined flexion (15 degrees) and extension (5 degrees) deficit noted in 1 patient. Normal range of motion was observed in 83% (25/30) patients.</td>
<td>No complications related to the device were reported.</td>
<td>Follow-up issues:
• Not reported
Study design issues:
• Method of patient recruitment not reported.
• Validated methods of outcome assessment for functional activity (Lysholm; Tegner) and pain (VAS). Functional levels also assessed with WOMAC. Scores range from 0 (worst) to 100 (best).
• Statistical analysis using Wilcoxon nonparametric tests. No statistical analysis was performed for the lateral CMI study on account of small sample size.

Other issues:
Physical therapy started form first postoperative day and followed for 6 months until full recovery of daily life activity achieved.</td>
</tr>
</table>

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Case series 2
Recruitment period: not reported
Study population:
Patients undergoing partial replacement of the lateral meniscus.

n=12
Age: range 16–40 years
Sex: not reported
Patient selection criteria: not reported
Technique: partial replacement of the lateral meniscus with an implant (Lateral CMI, ReGen). Patient is placed in a supine position with the knee at 90 degrees of flexion. Following preparation of the implant site, the anterior and the posterior attachment points are trimmed in a square shape to accept the scaffold. The dehydrated implant in a sterile package is measured, trimmed to fill the defect and inserted into the defect by using a vascular clamp. The stability of the implant was tested with a probe.

Follow-up: mean 20 months
Conflict of interest/source of funding: not reported</td>
<td>Case series with patients undergoing partial replacement of the lateral meniscus:
Number of patients analysed:12

Functional activity
<table>
<tr><th></th><th>Pre -operative</th><th>Follow-up</th><th>p value</th></tr>
<tr><td>Lysholm score</td><td>68.2 (13.9)</td><td>95.2 (5.8)</td><td>NR</td></tr>
<tr><td>Tegner activity</td><td>3.2 (1.7)</td><td>6.0 (2.2)</td><td>NR</td></tr>
<tr><td>WOMAC</td><td>NR</td><td>NR</td><td>NR</td></tr>
</table>
Data reported as mean (SD)
All patients were able to return to their usual daily life activities without any limitation in a mean time of 3 months after surgery.
Pain
<table>
<tr><th></th><th>Pre-operative</th><th>Follow-up</th><th>p value</th></tr>
<tr><td>VAS</td><td>8.8 (7.4)</td><td>2.3 (1.8)</td><td>NR</td></tr>
</table>
*Absence of pain reported in 8 patients

Restriction in range of motion
Compared with the opposite leg, range of motion was normal in all patients.</td>
<td>No complications related to the device were reported</td>
<td>Follow-up issues:
• Not reported
Study design issues:
• Method of patient recruitment not reported.
• Validated methods of outcome assessment for functional activity (Lysholm; Tegner) and pain (VAS). Functional levels also assessed with WOMAC. Scores range from 0 (worst) to 100 (best).
• Statistical analysis not performed on account of small sample size.
Other issues:
• Physical therapy started from first postoperative day and followed for 6 months until full recovery of daily life activity achieved.</td>
</tr>
</table>

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments
Monllau JC(2011)[6] **Case series** Spain (patients included in the European Multicentre Prospective Study) Recruitment period: September 1997 to January 2000 Study population: Patient with either persistent medial compartmental joint line pain because of a previous sizable meniscus resection or a larger irreparable meniscus tear at arthroscopy n=25 Age: range 18.3–48.2 years Sex: 80% male Patient selection criteria: Patients with large irreparable meniscus tear or persistent medial compartmental pain were included. Patients with complete loss of the medial meniscus, lateral meniscus injuries, untreated instability, grade IV chondral lesions, inflammatory arthritis, collagen allergies, autoimmune disease, or pregnant were excluded. Technique: Partial replacement of the meniscus with an implant(CMI). Following a diagnostic arthroscopy, puncture holes were made through the meniscal bed rim extending into the vascular zone of the meniscus. Sizing of the defect was with a specially designed flexible rod introduced into a rigid cannula. The anteromedial portal was enlarged to facilitate the introduction of the implant	Number of patients analysed:**22** **Functional activity** Outcome: Lysholm score; Preoperative: 59.9 (30–90); At final follow-up: 87.56 (59–100); p: <0.001 At preoperative stage: 0% rated as excellent and 4% good At final follow-up: 29% rated as excellent; 54% good **Pain** Outcome: VAS; Preoperative: 5.5 (2–8); At final follow-up: 2(0–6); p: 0.005 Data expressed as mean (range). **Patient satisfaction** Patient satisfaction with the procedure was rated as 3.4. This was evaluated on a 4-point scale, where 0 indicated very dissatisfied, and 4 indicated very satisfied. **Reoperations** 8% (2/25) patients required surgical revision because of implant failure and allograft meniscal transplantation was performed.	**Implant failure** Implant failure, defined as infection caused by the implant or mechanical failure of the implant, was reported in 8% (2/25). **Knee swelling/effusion** Moderate effusion was reported at 1 week (n=3) and at 6 months (n=4) follow-up. No knee effusion was reported immediately postoperative and at the final follow-up examination. Knee swelling was reported in 32% (7/22) (timing of assessment unclear).	**Follow-up issues**: • 88% followed-up. Loss to follow-up was because of patients requiring allograft meniscal transplantation (n=2) and patient unavailability (n=1; unrelated to the procedure). **Study design issues**: • Method of patient recruitment not reported. • Valid method of outcome assessment for pain (VAS) and functional levels (Lysholm). Lysholm score (range 0–100) was interpreted as excellent (>94 points), good (84–94 points) fair (65–83 points) and poor (<65 points) **Study population issues**: • 56% (14/25) had undergone previous knee surgeries. Partial arthroscopic meniscectomy had been performed in 10 of those cases. In the remaining 4 cases, index procedures were ACL reconstruction and PM. **Other issues**: • Muscle and range of motion exercises initiated immediately postoperatively and unrestricted physical activity allowed by 6 months.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details	Key efficacy findings	Key safety findings	Comments
which was soaked in saline solution before implantation. A longitudinal posteromedial incision was made to safely retrieve suture devices securing the posterior aspect of the implant and upon completion of suturing, the stability of the implant was tested with a probe. Follow-up: **10.1 to 12.5 years** Conflict of interest/source of funding: not reported			• Mean age (range) of all patients enrolled in study was 29.2 years (18.3–48.2). For patients who returned for follow-up, mean age (range) was 42.3 years (23.1–58.2).

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details

Bulgheroni P (2010)[7]

Case series

Italy

Recruitment period: January 2001 to December 2003

Study population: patients with irreparably damaged medial meniscus or the presence of persistent pain after meniscectomy.

n=34

Age: range 22–58 years

Sex: 74% male

Patient selection criteria: Patients with Outerbridge grade IV chondral lesions, autoimmune diseases infection, other systemic diseases, collagen allergies and age>60 years excluded.

Technique: Partial replacement of the meniscus with an implant (CMI). Arthroscopy of the knee joint was performed through standard anterolateral and anteromedial portals. Damaged or pathologic tissue was removed, the implant was introduced into the joint through a cannula and fixed using non-absorbable sutures. One surgeon undertook all procedures.

Follow-up: **range 60–76 months**

Conflict of interest/source of funding: No conflicts of interests declared.

Key efficacy findings

Number of patients analysed:**28**

Functional and activity

Outcome*	Pre-operative	Post-operative	p
Lysholm score	58	94	<0.01
Tegner activity	2	5	<0.01

*at 2 years follow-up

Results confirmed by clinical examination with comparable scores at 5-year follow-up. Numerical values for 5-year follow-up not reported.

Reoperation

29% (8/28) patients underwent a second arthroscopic look at different time-points after index surgery; 7 months (n=4) and at 12,18,36 and 60 months.

Number of patients	Reasons for reoperation
2	For an HTO (implant had to be removed)
3	Onset of pain with no associated trauma
2	Occurrence of a joint trauma
1	Planned in advance

Evaluation of implant

Morphology evaluated with MRI. In second look arthroscopies in 8 patients, MRI showed that the implant appeared not to be completely resorbed. The implant was reduced in size but remained stable over time. Histological examination of biopsy (follow-up at 5 years) showed meniscus-like tissue with cells and vessels and a maturation of the regenerated tissue with resorption of the original scaffold.

Key safety findings

Nerve damage

1 patient complained of paraesthesia of the leg. This was not attributed to the implant-the infrapatellar branch of the saphenous nerve was included in the suture.

Degenerative joint changes

Assessed radiographically and rated on the Kellgren-Lawrence scale.

Grade	Extent of degeneration	n
0–1	Not present	18
2–3	evident	9
4	Severe osteoarthritis	1

Preoperative radiographs not available for all patients.

Other

Assessment by MRI at 5-year follow-up showed subchondral bone oedema of the femoral condyle (n=10) and oedema of the tibial plateau (n=3).

Comments

Follow-up issues:

- 83% followed-up. Reasons for exclusion from analysis: patients refused an injection of contrast fluid (n=4), did not follow rehabilitation protocol and had to undergo new knee arthroscopy (n=1) and a new trauma in the knee that caused implant failure (n=1).

Study design issues:

- Method of patient recruitment not reported.
- MRI and radiographic assessment was evaluated by an independent radiologist. Validated method of assessment for assessment of functional (Lysholm) and activity levels (Tegner).
- **Study population issues**:
- 14 patients had associated surgery: ACL reconstruction (n=11), HTO (n=2), microfracture for a chondral lesion (n=1)

Other issues:

Physical rehabilitation started on the first post-operative day and return to full unrestricted activity was allowed at 6 months.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities

Study details

Spencer S.J. (2012)[8]

Case series
UK

Recruitment period: 2008 to 2010

Study population: Patients with painful knee following partial meniscectomy.

n=24
Menaflex: n=13 (7 medial; 5 lateral)
Actifit: n=11 (7 medial: 4 lateral)
Age: mean 35 years

Sex: 75% male

Patient selection criteria: Patients who had previously undergone PM more than 12 months earlier and had pain interfering with work, light sport or ADL. Patients with acute tears were not considered for reconstruction. Initially no restriction on grade of chondral wear, but over the study period patients with Outerbridge grade 0–3 were accepted and grade 4 excluded.

Technique: Partial replacement of the meniscus with collagen implants (Menaflex, ReGen Biologics) or polyurethane scaffold (Actifit, Orteq), positioned by arthroscopy. No further details reported.

Follow-up: 24 months (Menaflex group); 18 months (Actifit group)

Conflict of interest/source of funding: not reported

Key efficacy findings

Number of patients analysed: 14 patients (9 collagen implant and 5 treated by polyurethane scaffold

Functional outcomes

In patients treated by collagen implant:

Scale	Baseline (n=11)	24 months (n=9)	p-value
Lysholm	61.8	82.9	0.003
Tegner activity	3.7	5.2	0.09
IKDC	48.1	71.8	0.002
KOOS			
Pain	60.3	88.8	0.0003
Symptoms	54.1	79.7	0.001
ADL	69.3	94	0.001
Sports	35	62.2	0.002
QoL	31.5	57	0.002

In patients treated by polyurethane scaffold:

Scale	Baseline (n=11)	24 months (n=5)	p-value
Lysholm	56.5	86.6	0.009
Tegner activity	3.8	4.4	0.45
IKDC	42.1	74	0.001
KOOS			
Pain	56.7	85.6	0.02
Symptoms	52.5	87.6	0.004
ADL	66.8	93	0.06
Sports	37.3	66	0.08
QoL	27.8	61.4	0.0005

Evaluation of implant

Second-look arthroscopy was undertaken in 14 patients (at a mean of 12.8 months after implantation). Patients treated by collagen implant (5/9) had less than 50% infill. In patients treated by polyurethane scaffold, 1 patient had less than 50% infill and the remaining 4 patients had more than 50% infill.

Key safety findings

Implant failure (torn scaffold) was reported in 1 patient who developed sudden onset of pain (19 months following collagen implant surgery). Patient was treated by polyurethane scaffold.

Comments

Follow-up issues:

- 40% followed up at 2 years. Reasons for loss to follow-up not reported.

Study design issues:

- Patient recruitment method not reported.

Study population issues:

Other issues:

- There are discrepancies within the text and tables regarding how many patients were treated by the procedures.
- 36% (8 patients) underwent additional procedures: high tibial osteotomy (n=3), distal femoral osteotomy (n=2), revision ACL reconstruction (n=1), lateral collateral ligament reconstruction (n=1), and microfracture of the tibia chondral surface (n=1).
- Tailored post-operative rehabilitation not reported.

Abbreviations used: ACL, anterior cruciate ligament; ADL, activities of daily living; CMI, collagen meniscus implant; HTO, high tibial osteotomy; IKDC, International Knee Documentation Committee; ITT, intention-to-treat; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCMI, medial collagen meniscus implant; NR, not reported ; PM, partial meniscectomy; PMM, partial medial meniscectomy; QoL, quality of life; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
	Progression in chondral wear No progression in chondral wear was noted on repeat MRI scanning (at a mean of 19 months after the procedure). Mean Outerbridge score at baseline: 1.9. Score not reported at follow-up.		

Efficacy

Pain relief

Two study arms were included in a randomised controlled trial (RCT) of 311 patients. One study arm of 157 patients who had no prior surgery (75 treated by partial replacement of the meniscus with an implant compared with 82 treated by partial meniscectomy) and a second study arm of 151 patients who had prior surgery (82 treated by partial replacement of the meniscus with an implant compared with 69 treated by partial meniscectomy) reported pain ratings. Pain was assessed (on a visual analogue scale from 0–100, with 0 indicating no pain and 100 indicating the worst possible pain) at rest, during activities of daily living and at the highest level of activity. Pain scores were reported as a mean change from the preoperative score. In the first study arm (n=157) mean pain scores were 16 and 21 for the implant and the partial meniscectomy groups, respectively. In the second study arm (n=151), the mean pain score was 18 for both the implant and the partial meniscectomy groups. These differences were reported as not significant (p-values not reported). Mean follow-up was 59 months[1].

A non-randomised study of 33 patients, treated by partial replacement of the medial meniscus with an implant (n=17) or partial medial meniscectomy (n=16) reported scores for knee pain assessed during rest and activity (assessed on a visual analogue scale from 0–10, with 0 indicating no pain and 10 indicating the worst possible pain). Mean pain score was 1 (SD 1) and 3 (SD 2) for the implant and the partial meniscectomy groups, respectively. This difference was significant (p=0.004) (mean follow-up period of 133 months)[3].

Functional mobility

Functional assessment

The RCT of 311 patients reported results for knee function assessed using the Lysholm scale (assessed on a scale ranging from 0–100, with higher numbers corresponding to better function). Functional scores were reported as a mean change from the preoperative score. Mean follow-up was 59 months[1]. In the first study arm in patients who had no prior surgery (n=157; 75 treated by partial replacement of the meniscus with an implant compared with 82 treated by partial meniscectomy) functional scores were 26 and 28 for the implant and the partial meniscectomy groups, respectively. This difference was reported as not significant (p value not reported). In the second study arm in patients who had prior surgery (n=151; 82 treated by partial replacement of the meniscus with an implant compared with 69 treated by partial meniscectomy) functional scores were 16 and 22 for the implant group and the partial meniscectomy group, respectively. This difference was reported as not significant (p value not reported).

An RCT of 60 patients, which included 30 patients treated by the procedure and high tibial osteotomy (there was a high dropout rate in the comparator arm of tibial osteotomy alone) reported that the 23 patients followed for 8–18 months had Lysholm scores which improved from 65 to 94 (p-value not reported).

A case series of 34 patients reported mean functional scores in patients treated by partial replacement of the meniscus with an implant. The mean functional score (measured by Lysholm scale) improved significantly, from 58 before the procedure to 94 ($p<0.01$) at the 2-year follow-up[7].

A case series of 25 patients, who were treated by a partial replacement of the meniscus with an implant, reported functional scores. The mean Lysholm scale improved significantly from 60 preoperatively to 88 ($p<0.001$) at the final follow-up (follow-up of 10 to 13 years)[6].

A case series of 52 patients treated by partial replacement of the meniscus with a polyurethane scaffold reported that mean functional scores (measured by the Knee Injury and Osteoarthritis Outcome Score on a scale of 0–100, with higher numbers corresponding to better function) increased significantly from baseline for the following five subscales: symptoms (from 65 to 78), pain (from 58 to 79), activities of daily living (from 69 to 84), sports (from 31 to 59) and quality of life (from 34 to 57) at 24-months follow-up ($p<0.0001$)[4].

A case series of 24 patients reported that mean functional scores (measured by the International Knee Documentation Committee scale from 0–100, with higher numbers corresponding to better function) improved significantly, from 48 before the procedure to 72 at 2-year follow-up ($p=0.002$) in patients treated by collagen implant ($n=9$) and from 42 before the procedure to 74 at 18-months follow-up ($p=0.001$) in patients treated by polyurethane scaffold ($n=5$)[8].

Activity levels

The case series of 34 patients reported mean Tegner activity score (assessed on a scale from 0 (indicating patient disability) to 10 (indicating participation in competitive sports). Activity levels improved significantly ($p<0.01$) from 2 at preoperative examination to 5 at the 2 year follow-up[7].

One study reported results for functional assessment from 2 case series[5]. A case series of 30 patients treated by partial replacement of the meniscus with an implant (medial side) reported a significant improvement in the mean Tegner activity score from 4 (SD 2) preoperatively to 5 (SD 2) postoperatively ($p=0.004$) at a mean follow-up of 8 years[5]. A case series of 12 patients, who were treated by partial replacement of the meniscus with an implant (lateral side) reported an improvement in the mean Tegner activity score from 3 (SD 2) before the procedure to 6 (SD 2) at last follow-up (mean follow-up 20 months). Statistical analysis was not carried out because of the small number of patients included in the study[5].

Improvement of range of motion

One study reported results for changes in range of motion from 2 case series[5]. The case series of 30 patients reported a normal range of motion (compared with the opposite leg) in 86% (26/30) of the patients at mean follow-up of 8 years[5]. The case series of 12 patients reported a normal range of motion (compared with the opposite leg) in all patients at last follow-up (mean follow-up 20 months)[5].

Quality of life

The non-randomised study of 33 patients treated by partial replacement of the medial meniscus (n=17) or by partial medial meniscectomy (n=16) reported mean quality of life scores (assessed using a self-administered SF-36 questionnaire for physical and mental health; scale 0–100, higher score indicating better function). Mean SF-36 scores for the physical health index were 54 (SD 4) and 44 (SD 9) for the implant and the partial meniscectomy groups, respectively. This difference was significant (p=0.026). Mean SF-36 scores for the mental health index were 55 (SD 4) and 44 (SD 7) for the implant and the partial meniscectomy groups, respectively. This difference was significant (p=0.004; mean follow-up period of 133 months)[3].

Need for further surgery

The RCT of 311 patients reported reoperation rates. Results for the two study arms were not reported separately. Reoperation was defined as an additional surgical procedure (outside the protocol) on the knee as a result of disabling or persistent pain and/or mechanical symptoms that could possibly involve the meniscus[1].

The reoperation rates were 10% and 3% for the implant and the partial meniscectomy groups respectively, at 5 years (denominators not reported; p-values not reported). In 3 patients, the primary surgical procedure performed was explantation of the implant. Reasons for reoperation included pain, swelling and instability[1].

The non-randomised study of 33 patients treated by partial replacement of the medial meniscus (n=17) or by partial medial meniscectomy (n=16) reported the need for further surgery in 2 patients in each group (mean follow-up period of 133 months). Reasons for reoperation were pain and swelling[3].

Patient satisfaction

The RCT of 311 patients reported patient satisfaction with the current condition of their knee. Patient satisfaction was rated on a 5-point scale, with responses ranging from very dissatisfied to very satisfied (mean follow-up 59 months). In the first study arm in patients who had no prior surgery (n=157; 75 treated by partial replacement of the meniscus with an implant compared with 82 treated by partial

meniscectomy) 82% and 75% of the patients were ‘very/somewhat satisfied’ in the implant and the partial meniscectomy groups, respectively. This difference was not significant (p>0.05). In the second study arm in patients who had prior surgery (n=151; 82 treated by partial replacement of the meniscus with an implant compared with 69 treated by partial meniscectomy) 66% of the patients in the implant group and 49% of the patients in the partial meniscectomy group were ‘very/somewhat satisfied’ with the current condition of their knee at a mean follow-up at 59 months. This difference was not significant (p=0.09)[1].

The case series of 25 patients reported patient satisfaction with the procedure as 3.4 (evaluated on a 4-point scale; 0 indicating very dissatisfied, to 4 indicating very satisfied).The range of follow-up was 10 to 13 years[6].

Technical efficacy

The RCT of 311 patients reported no failures caused by a lack of healing of the implant to the meniscus rim or gross tearing of the implant[1].

Explantation of the implant (because of mechanical failure) was performed in 1% (1/75) of the patients in the first study arm of 157 patients who had no prior surgery (75 treated by partial replacement of the meniscus with an implant compared with 82 treated by partial meniscectomy). Explantation was performed in 2% (2/82) of the patients in the second study arm of 151 patients who had prior surgery (82 treated by partial replacement of the meniscus with an implant compared with 69 treated by partial meniscectomy; causes not reported). The timing of when the patient underwent reoperation for removal of the implant was unclear[1].

In a case series of 52 patients, during relook arthroscopy at 12 months, non-integration of the polyurethane scaffold with the native meniscus was observed in 2 patients[4].

In the case series of 52 patients treated by partial replacement of the meniscus with a polyurethane scaffold, treatment failure (defined as additional surgical procedure on the involved meniscus) was reported in 15% (8/52) of patients (treatment failure related to infection was excluded) and the overall treatment failure was 17% (9/52). Three cases were definitely related to the implant, 3 were not related to the implant, 1 was possibly related to the implant, 1 was unknown and 1 treatment failure (infection) was not related to the implant. Timing to the need for further intervention ranged from 1week to 24 months[4].

Safety

Leg paraesthesia/nerve injury

Nerve injury and numbness were reported in 1 patient in each group (denominator not reported) in the RCT of 311 patients (partial replacement of the meniscus compared with partial meniscectomy). The timing of assessment was unclear[1].

Paraesthesia of the leg in 1 patient was reported in the case series of 34 patients. It was reported that this was related to the saphenous nerve included in the tying of the suture[7].

Dislocation of the implant

Dislocation of the implant was reported in 4% (1/23) in an RCT of 60 patients (30 treated by partial replacement of the meniscus with an implant combined with high tibial osteotomy compared with 30 treated by high tibial osteotomy alone) at 8 to 18 months after surgery. The implant had to be removed[2].

Infection

A skin infection was reported in 1 patient in the implant group at 1 week in the RCT of 311 patients (patients treated by partial replacement of the meniscus compared with partial meniscectomy). This was not considered to be directly related to the implant. The infection penetrated into the joint resulting in the removal of the implant[1].

Postoperative infection (unrelated to the polyurethane scaffold) was reported in 1 patient in the case series of 52 patients at 1 week after the index surgery (resolved with treatment; no further details reported)[4].

Implant failure (defined as infection caused by the collagen implant or mechanical failure of the implant) was reported in 8% (2/25) of the patients in the case series of 25 patients (during follow-up of 10 to 13 years)[6]. Results for the number of patients with infections and the number of technical failures of the implant were not reported separately.

Knee swelling/effusion

Swelling, effusion and redness were reported in 4 patients treated by partial replacement of the meniscus by an implant and in 1 patient treated by partial meniscectomy in the RCT of 311 patients (timing of assessment was unclear; denominator not reported)[1].

Knee swelling was reported in 32% (7/22) of the patients in the case series of 25 patients who received a collagen implant (timing of assessment was unclear; further details not reported)[6].

Pain

Pain was reported in 2 patients treated by partial replacement of the meniscus and 7 treated by partial meniscectomy in the RCT of 311 patients (denominator not reported). Patients needed further operations (no further details reported). The timing of assessment was unclear[1].

Swelling and pain were reported in 6% of the patients who received an implant in a non-randomised study of 33 patients (17 treated by partial replacement of the meniscus with an implant compared with 16 treated by partial medial meniscectomy). The timing of assessment was unclear; absolute numbers were not reported. The study reported that these events were assumed to be related to the implant[3].

Validity and generalisability of the studies

- There were differences in the postoperative rehabilitation protocol and duration of the rehabilitation period between the group treated by partial replacement of the meniscus and the comparative group in different studies.
- The age of patients included in the studies ranged from 16 to 68 years. Where reported, most patients were men.
- Follow-up ranged from 12 months to 12.5 years.
- The number of concomitant surgical procedures varied between the studies. This makes the evaluation of partial replacement of the meniscus of the knee as a stand-alone treatment challenging.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Individually magnetic resonance imaging-designed unicompartmental interpositional implant insertion for osteoarthritis of the knee. NICE interventional procedures guidance 317 (2009). Available from www.nice.org.uk/guidance/IPG317
- Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis. NICE interventional procedures guidance 230 (2007). Available from www.nice.org.uk/guidance/IPG230

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr Timothy Briggs (British Association for Surgery of the Knee), Mr Andrew Porteous and Mr Andrew Price (British Orthopaedic Association).

- Two Specialist Advisers have performed the procedure at least once and one Specialist Adviser has never performed this procedure.
- All Specialist Advisers considered the procedure to be novel and of uncertain safety and efficacy.
- One Specialist Adviser noted that the comparators were allograft meniscal transplant or no further treatment, which would be likely to increase arthritis risk.
- Key efficacy outcomes: pain reduction, functional improvement, reduction of the risk of further degeneration of the articular cartilage lining of the knee, early failure (further surgery) and early failure (symptoms/patient-related outcome measures [PROM]).
- One Specialist Adviser listed theoretical adverse events to be: reaction to foreign material, lack of repair/healing with subsequent tearing or displacement, infection or standard related risks for any knee surgery operation.
- Two Specialist Advisers noted there is uncertainty about the indications for the procedure. One Specialist Adviser indicated that the threshold of symptoms at which the procedure can be performed and whether this procedure should be considered prophylactically in young patients if significant meniscal tissue was removed is uncertain.
- All of the Specialist Advisers noted that there is uncertainty about the efficacy of the procedure and one stated that long-term reduction in osteoarthritis risk is uncertain.
- Two Specialist Advisers noted that surgeons need to be experienced in meniscal repair to undertake this procedure safely and one noted it should

be limited to specific surgeons (specialist knee surgeons in regional centres).

- In terms of numbers of patients eligible for treatment and use of resources and the potential impact on the NHS, one Specialist Adviser thought this procedure would have a major impact, one Specialist Adviser thought the impact would be moderate and one Specialist Adviser thought the impact would be minor.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- The studies related to the different implants used for the procedure (7 studies examined collagen implants (derived from animal collagen) and 1 study examined polyurethane scaffold).

References

1. Rodkey WG, DeHaven KE, Montgomery WH III et al. (2008) Comparison of the collagen meniscus implant with partial meniscectomy. A prospective randomized trial. Journal of Bone and Joint Surgery 90(7): 1413–26

2. Linke RD, Ulmer M and Imhoff AB (2006) Replacement of the meniscus with a collagen implant (CMI). Operative Orthopadie und Traumatologie 18 (5–6): 453–462

3. Zaffagnini S, Marcheggiani Muccioli GM, Lopomo Net al. (2011) Prospective long-term outcomes of the medial collagen meniscus implant versus partial medial meniscectomy: a minimum 10-year follow-up study. American Journal of Sports Medicine 39(5): 977–85

4. Verdonk R, Beaufils P, Bellemans J et al. (2012) Successful treatment of painful irreparable partial meniscal defects with polyurethane scaffold: two-year safety and clinical outcomes. American Journal of Sports Medicine 39(4): 774–82

5. Zaffagnini S, Marcheggiani Muccioli GM, Giordano G et al. (2009) Synthetic meniscal scaffolds. Techniques in Knee Surgery 8(4): 251–6

6. Monllau JC, Gelber PE, Abat F et al. (2011) Outcome after partial medial meniscus substitution with the collagen meniscal implant at a minimum of 10 years' follow-up. Arthroscopy 27(7): 933–43

7. Bulgheroni P, Murena L, Ratti C et al. (2010) Follow-up of collagen meniscus implant patients: clinical, radiological, and magnetic resonance imaging results at 5 years. Knee 17(3): 224–9

8. Spencer SJ, Saithna A, Carmont MR et al. (2012) Meniscal scaffolds: Early experience and review of the literature. Knee [Epub ahead of print], doi:1.1015/j.knee.2012.01.006

Appendix A: Additional papers on partial replacement of the meniscus of the knee using a biodegradable synthetic polymer scaffold

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Efe T, Getgood A, Schofer MD et al. (2011) The safety and short-term efficacy of a novel polyurethane meniscal scaffold for the treatment of segmental medial meniscus deficiency. Knee Surgery, Sports Traumatology, Arthroscopy [Epub ahead of print, identified by consultee]	n=10 Follow up =12 months	At 6 months, a statistically significant improvement ($p<0.05$) in all patient-related outcome measures except the University of California Los Angeles (UCLA) activity scale and visual analogue pain scale were noted. The improvement remained at 12 months. MRI analysis revealed the presence of scaffolds at 6 months, with evidence of some tissue integration and many improvements in scaffold morphology and International Cartilage Repair Society classification of cartilage in the medial compartment were noted at 12 months. No synovitis was noted in the joint or adverse reactions in the other compartments.	Larger studies included in table 2.

Genovese E, Angeretti MG, Ronga M et al. (2007) Follow-up of collagen meniscus implants by MRI. Radiologia Medica 112(7): 1036–48	n=40 Follow up=24 months	Implant completely resorbed with free prosthetic fragments in 1 patient. Reduction in implant size in 37.5% of patients at 24 months.	Larger studies included in table 2.
Gomoll AH, Filardo G, Almqvist FK et al (2012) Surgical treatment for early osteoarthritis. Part II: allografts and concurrent procedures Knee Surgery, Sports Traumatology, Arthroscopy 20: 468–486	n=not applicable Follow up= not applicable	Cartilage repair has become a focus of increased interest due to its potential to provide pain relief and alter the progression of degenerative disease, with the hope of delaying or obviating the need for joint replacement. The field of cartilage repair is seeing the rapid development of new technologies that promise greater ease of application, less demanding rehabilitation and better outcomes. Concurrent procedures such as meniscal transplantation and osteotomy, however, remain of crucial importance to provide a normalised biomechanical environment for these new technologies.	Review.
Harston A, Nyland J, Brand E, et al. (2011) Collagen meniscus implantation: a systematic review including rehabilitation and return to sports activity Knee Surgery, Sports Traumatology, Arthroscopy 20(1): 135–46. Epub	n= 11 studies Follow up = not applicable	Based primarily on Lysholm Knee Score, Tegner Activity Scale, pain scales and self-assessment measurements, knee function, symptoms, and activity level generally improved by 46.6 ± 39.9 months post-surgery. Reduced collagen implant size at last follow-up was reported in 6/11 (54.5%) studies, but the significance of this finding is unknown. Knee function, symptoms, and activity level generally improved following CMI use, but poor research report quality was common. Additional well-designed	The studies and outcomes reported in the systematic review have been included in the overview. Searches were limited from 1995 onwards and have not captured all the studies identified in table 2 and appendix A.

		long-term prospective studies are needed to better determine knee osteoarthritis prevention efficacy and appropriate patient selection.	
Laprell H and Verdonk R. (2010) Clinical Efficacy and tissue ingrowth following implantation of an a vascular synthetic scaffold for treatment of irreparable meniscus tears. Journal of Bone and Joint Surgery British Volume 93-B, Issue SUPP_II, 160. EFORT - European Federation of National Associations of Orthopaedics and Traumatology (11th Congress)	n=52 Follow up = 12 months	Dynamic contrast magnetic resonance Imaging (DCMRI) and relook arthroscopy findings illustrate biocompatibility. Tissue ingrowth and biopsy results show potential for differentiation into meniscus-like tissue. Importantly subjects experienced significant pain relief and were able to resume normal activities. No safety concerns have been raised.	Conference publication. Potential overlap of patients in Verdonk 2011 (in appendix A) and Verdonk 2012 (table 2).
Mouzopoulos G, Siebold R .(2012) Partial meniscus substitution with tissue-engineered scaffold: an overview Clinics in Sport Medicine 31: 167–181	n=not applicable Follow up = not applicable	Prospective, randomised studies with long-term follow-up are needed, comparing both meniscal scaffolds and control patients after partial meniscectomy to provide evidence-based knowledge about the clinical efficacy. Also, long-term MRI studies could be helpful in determining the integrity of the scaffolds over time.	Review.
Reguzzoni M, Manelli A, Ronga M et al. (2005) Histology and ultrastructure of a tissue-engineered collagen meniscus before and after implantation. Journal of Biomedical Materials Research Part (2): 808–816	n=4 Follow-up: 6 months	Lysholm score and Tegner activity score increased in all operated knees during the follow-up.	Larger studies with longer length of follow-up included in table 2.
Ronga M, Bulgheroni P, Manelli A et al. (2003) Short-term evaluation of collagen meniscus implants by MRI and morphological analysis. Journal of Orthopaedics and Traumatology 4 (1): 5–10	n=2 Follow-up: 12 months	The biopsy specimens demonstrated invasion of the scaffold by connective tissue and blood vessels. Magnetic Resonance Imaging findings confirmed collagen implant biocompatibility and supported the hypothesis that collagen	Larger studies included in table 2.

		implant stimulates regeneration of meniscal-like tissue.	
Steadman JR and Rodkey WG (2005). Tissue-engineered collagen meniscus implants: 5- to 6-year feasibility study results. Arthroscopy 21(5): 515–525	n=8 Follow-up: 5.5 to 6.3 years	Lysholm and Tegner activity scores improved significantly compared with preoperative status and remained unchanged compared with 2 year evaluations.	Larger studies included in table 2.
Verdonk R, Verdonk P, Huysse W et al. (2011) Tissue ingrowth after implantation of a novel, biodegradable polyurethane scaffold for treatment of partial meniscal lesions. American Journal of Sports Medicine 39(4): 774–82	n=52 Follow up = 12 months	Non-integration of the scaffold with the native meniscus was reported in 1 patient at 12-month follow up. No serious adverse reaction to the scaffold material reported.	Interim report of Verdonk (2012) included in table 2.
Zaffagnini S, Giordano G, Vascellari, A et al.(2007) Arthroscopic collagen meniscus implant results at 6 to 8 years follow up. Knee Surgery, Sports Traumatology, Arthroscopy 15(2): 175–183	n=8 Follow-up: 6.8 years	Both subjective Cincinnati Knee Rating System (CKRS) score and objective IKDC score showed improvement. Absence of pain remained for 6 years after surgery in four cases.	Larger studies included in table 2.

Appendix B: Related NICE guidance for partial replacement of the meniscus of the knee using a biodegradable synthetic polymer scaffold

Guidance	Recommendations
Interventional procedures	**Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis. NICE interventional procedures guidance 230 (2007)** 1.1 Evidence on the safety and efficacy of arthroscopic knee washout with debridement for the treatment of osteoarthritis is adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 Current evidence suggests that arthroscopic knee washout alone should not be used as a treatment for osteoarthritis because it cannot demonstrate clinically useful benefit in the short or long term.
	Individually magnetic resonance imaging-designed unicompartmental interpositional implant insertion for osteoarthritis of the knee. NICE interventional procedures guidance 317 (2009) 1.1 Current evidence on the safety and efficacy of individually magnetic resonance imaging (MRI)-designed unicompartmental interpositional

	implant insertion for osteoarthritis of the knee is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research studies. These should include clear descriptions of patient selection; and should report both objective and patient-reported outcomes and the length of time before joint replacement is required. 1.2 NICE may review the procedure on publication of further evidence.

Appendix C: Literature search for partial replacement of the meniscus of the knee using a biodegradable synthetic polymer scaffold

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	15/03/2012	Issue 3 of 12, Mar 2012
Database of Abstracts of Reviews of Effects – DARE (CRD website)	15/03/2012	n/a
HTA database (CRD website)	15/03/2012	n/a
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	15/03/2012	Issue 3 of 12, Mar 2012
MEDLINE (Ovid)	15/03/2012	1946 to March Week 1 2012
MEDLINE In-Process (Ovid)	15/03/2012	March 14, 2012
EMBASE (Ovid)	15/03/2012	1980 to 2012 Week 10
CINAHL (NLH Search 2.0/EBSCOhost)	15/03/2012	1981 to present
	15/03/2012	n/a

MEDLINE search strategy

The MEDLINE search strategy was adapted for use in the other sources.

Strategy used:

1 Menisci, Tibial/

2 ((menisc$ or knee$ or cartilage$) adj3 (injur$ or damage$ or stress$ or loss$ or lesion$ or lock$ or torn$ or tear$ or overuse$ or sport$)).tw.

3 ((semilunar or semi-lunar or (semi adj1 lunar)) adj3 cartilage$).tw.

4 "loos$ bod$".tw.

5 or/1-4

6 Knee Injuries/

7 Knee Joint/

8 or/6-7

9 Arthroscopy/

10 arthroscop$.tw.

11 or/9-10

12 8 and 11

13 Tissue Scaffolds/

14 Guided Tissue Regeneration/

15 Absorbable Implants/

16 Biocompatible Materials/

17 Coated Materials, Biocompatible/

18 Polyurethanes/

19 ((menisc$ or tissue$ or collagen or polyurethane$ or biodegradable or absorbable or bioabsorbable or biocompatible or biomaterial$ or hemocompatible) adj3 (implant$ or scaffold$ or polymer$ or regenerat$ or re-generat$)).tw.

20 or/13-19

21 (actifit or menaflex).tw.

22 5 and 20

23 12 and 20

24 or/21-23

25 animals/ not humans/

26 24 not 25

27 limit 26 to english language

28 limit 27 to yr="2001 -Current"