NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of joint distraction for knee osteoarthritis without alignment correction

Osteoarthritis of the knee is caused by deterioration of the cartilage and underlying bone in the knee joint, resulting in stiffness, swelling, pain and difficulty in walking. In joint distraction for knee osteoarthritis without alignment correction, an operation is done to separate the bones on either side of the knee joint and an external frame is fixed to these bones to hold them apart and allow the damaged cartilage to heal.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) 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 IP overview was prepared in December 2014.

Procedure name

- Joint distraction for knee osteoarthritis without alignment correction

Specialist societies

- British Association for Surgery of the Knee
- British Limb Reconstruction Society

Description

Indications and current treatment

Osteoarthritis of the knee is the result of progressive deterioration of the articular cartilage and menisci of the joint. Articular cartilage deteriorates because of injury, or wear and tear. This leads to exposure of the bone surface. Symptoms include pain, stiffness, swelling and difficulty walking.

Treatment for knee osteoarthritis depends on the severity of the disease. Conservative treatments include analgesics and corticosteroid injections to relieve pain and inflammation, and physiotherapy and prescribed exercise to improve function and mobility. When symptoms are severe, surgery may be indicated. Options include upper tibial osteotomy, microfracture surgery, and unicompartmental or total knee replacement.

What the procedure involves

Joint distraction for knee osteoarthritis without alignment correction aims to offload and modify the mechanical environment in osteoarthritic joints to allow cartilage regrowth. Intra-articular surgery (such as debridement) may be done before distraction to stimulate cartilage healing.

With the patient under spinal block or general anaesthesia, pins are drilled through the tibia and femur. A distraction frame is then fitted external to the leg, unloading the knee by gradually increasing the distance between the cartilaginous surfaces of the knee (usually up to 5 mm) over a few days or weeks. The distraction is normally maintained for about 2-3 months before the frame is removed. During this time the patient is able to walk. The continuous flow of synovial fluid through the joint (enhanced by the distraction) is claimed to support chondrocyte nutrition and regeneration of cartilage. However, the exact mechanisms that may lead to cartilage regeneration during distraction are not known.

Osteoarthritis classification

Kellgren–Lawrence grading system

The Kellgren–Lawrence grading system uses radiographic images from X-rays to classify osteoarthritis according to the degree of joint space narrowing and the presence of osteophytes, which are small bony projections that form around joint margins that limit joint mobility and cause pain. The system consists of 5 categories:

- grade 0: normal cartilage
- grade 1: possible osteophytes and unlikely joint space narrowing

- grade 2: small osteophytes and possible joint space narrowing
- grade 3: multiple, moderately sized osteophytes, definite joint space narrowing, some sclerotic areas, possible deformation of bone ends
- grade 4: multiple large osteophytes, severe joint space narrowing, marked sclerosis and definite bony end deformity.

Outcome measures

Western Ontario and McMaster Universities Arthritis Index

The Western Ontario and McMaster Universities Arthritis Index (WOMAC) is an extensively used standardised questionnaire that is used to assess patients with osteoarthritis of the knee or hip. The questionnaire evaluates 3 domains: pain (score range 0–20); stiffness (score range 0–8) and physical function (score range 0–68). The total score ranges from 0 to 96 with lower scores indicating better outcomes.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to joint distraction for knee osteoarthritis without alignment correction. Searches were conducted of the following databases, covering the period from their commencement to 2 December 2014: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was 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 knee osteoarthritis.
Intervention/test	Joint distraction without alignment correction.
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 IP overview

This IP overview is based on 87 patients from 1 non-randomised comparative study[1] and 2 case series[2,3].

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 joint distraction for knee osteoarthritis without alignment correction

Study 1 Aly TA (2011)

Details

Study type	Non-randomised comparative study
Country	Egypt
Recruitment period	2003-2005
Study population and number	n=**61 (19 joint distraction and debridement versus 42 debridement alone)** patients with knee osteoarthritis.
Age and sex	Range 39-68 years; 69% (42/61) female
Patient selection criteria	Patients with knee osteoarthritis who refused common surgical procedures including total knee arthroplasty and high tibial osteotomy were included in the joint distraction group.
Technique	• Joint distraction group: debridement and abrasioplasty of the large ulcers of both femoral and tibial condyles were performed through anterolateral and anteromedial portals, then lavage and drilling of the cartilage defects of the knee were done. An Ilizarov external fixator was applied to all patients: 1.5 rings above and 1.5 rings below the knee joint. Distraction of the joint was done through the threaded rods on both sides, 1 mm per day for 4 weeks, starting from the first day. Ambulation was allowed with full weight bearing of the affected limb when total distraction was reached after 4 weeks. The external fixator was removed after 3 months. • Debridement-only group: treatment began with lavage to rid the joint of debris, then arthroscopic debridement was performed. Patients started aided walking on the second postoperative day for 8 weeks. All patients were treated conservatively for 3 to 6 months with analgesic anti-inflammatory medication, physiotherapy, and modification of activities of daily living. Antibiotic prophylaxis was given for 24 hours, as well as antithrombotic prophylaxis (heparin 5000 IU daily) until discharge from the hospital. Early active exercises of the knee and quadriceps were started from the second postoperative day.
Follow-up	**Range 3-5 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues:

- All patients had both clinical and radiological examination preoperatively and throughout the follow-up period.
- All patients had regular assessment every 2 weeks for the first 3 months, monthly until the end of the first year, then every 6 months until the end of the follow-up period, which ranged from 58 to 82 months (average, 65 months) for the joint distraction group. In the debridement-only group, follow-up ranged from 43 to 72 months (average, 52 months).

Study design issues:

- The patients who were included in the joint distraction group had refused common surgical procedures for osteoarthritis.
- Data were analysed with the Student t test.
- Only within-group (before-after) statistical tests undertaken.

Study population issues:

- Patient weight in the joint distraction group: 70-95 kg; patient weight in the debridement-only group: 65-80 kg.
- In the joint distraction group: 58% (11/19) of patients had unstable meniscal tears. All had degenerative ulcers in their femoral and/or tibial condyles.

Other issues: None.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **61 (19 versus 42)**

Improvement in pain*

	No pain (score=0)	Mild pain (score=1)	Moderate pain (score=2)	Severe pain (score≥3)
Joint distraction group (n=19)				
Preoperatively			53% (10/19)	47% (9/19)
After 3 months		63% (12/19)	26% (5/19)	11% (2/19)
After 1 year		74% (14/19)	21% (4/19)	5% (1/19)
End of follow-up period (range 58-82 months)	58% (11/19)**	31% (6/19)	10% (2/19)	
Debridement-only group (n=42)				
Preoperatively		29% (12/42)	46% (27/42)	7% (3/42)
End of follow-up period (range 43-72 months)	50% (21/42)***	30% (13/42)	13% (5/42)	7% (3/42)

*Pain score measured on a 4-point Likert scale, with a higher score indicating more severe pain.

**Significant improvement in pain from baseline observed within group (p<0.004)

*** No significant improvement in pain from baseline observed within group (p=0.163)

- Pain markedly increased during the first 5 days of joint distraction.
- Positive correlation between body weight and persistence of pain postoperatively and at final follow-up (p=0.038).

Walking capacity

	Walking capacity range (min) in the joint distraction group (n=19)	Walking capacity range (min) in the debridement-only group (n=42)
Preoperatively	10-35	12-23
End of follow-up period	32-51*	20-31**

*Significant improvement in walking capacity observed within group (p<0.001)

**No significant improvement in walking capacity observed within group (p=0.142)

Safety

Complications

	% of patients in the joint distraction group (n=19)	Other
Pin tract infections	18% (absolute number not given)	All patients responded completely to local cleaning and systemic antibiotics.
Deep vein thrombosis	11% (2/19)	In 1 patient, the thrombosis resolved after heparinisation, but the other patient developed non-fatal pulmonary embolism.

Stair climbing

	% of patients in the joint distraction group **preoperatively** (n=19)	% of patients in the joint distraction group at **final follow-up** (n=19)	% of patients in the debridement-only group **preoperatively** (n=42)	% of patients in the debridement-only group at **final follow-up** (n=42)
No difficulty	0	74% (14/19)*	33% (13/42)	67% (28/42)**
Some difficulty	100% (19/19)	26% (5/19)	67% (29/42)	33% (14/42)

*Significant improvement in stair climbing observed within group (p<0.002)

**Significant improvement in stair climbing observed within group (p<0.001)

Knee motion (degree)

	Knee motion range (degree) in the joint distraction group (n=19)	p value	Knee motion range (degree) in the debridement-only group (n=42)	p value
Active flexion				
Preoperatively	75-95		80-110	
End of follow-up period	110-135	**0.029**	100-110	0.153
Passive flexion				
Preoperatively	85-120		80-120	
End of follow-up period	150-170	0.193	90-130	0.142

Average joint space

	Average joint space (mm) in the joint distraction group (n=19)	Average joint space (mm) in the debridement-only group (n=42)
Preoperatively	2.5	2.7
End of follow-up period	4.3*	2.4**

*Significant improvement in average joint space observed within group (p<0.001)

**No significant difference observed within group (p=0.135)

Tibiofemoral angle

	Tibiofemoral angle range (degree) in the joint distraction group (n=19)	Tibiofemoral angle range (degree) in the debridement-only group (n=42)
Preoperatively	173-189	170-185
End of follow-up period	171-174*	No change

*Significant improvement observed within group (p<0.001)

Study 2 Wiegant K (2013)

Details

Study type	**Case series**
Country	Netherlands
Recruitment period	2006
Study population and number	n=**20** successive patients with end-stage knee osteoarthritis (OA) and an indication for total knee replacement.
Age and sex	Mean 49 years; 45% (9/20) female
Patient selection criteria	Age below 60 years, Visual Analogue Scale (VAS) of pain≥60 mm, and radiographic signs of primarily tibiofemoral OA joint damage. Exclusion criteria: severe symptoms in both knees, primary patella-femoral OA, a history of inflammatory or septic arthritis, severe knee misalignment (>10º) requiring surgical correction and inability to cope with an external fixator for 2 months.
Technique	An external fixation frame consisting of 2 monotubes with internal coil springs was placed, bridging the knee joint. Each monotube was fixed to 2 bone pins on each end and, in stages, distracted for 5 mm. Patients were allowed and encouraged to load the distracted joint with full weight-bearing capacity, supported with crutches. In case of superficial pin tract infections, treatment with oral antibiotics for 5-7 days was provided (flucloxacillin). Every 2 weeks, the patients returned to the hospital and the monotubes were temporarily removed. The knee was bent, for 3-4 h, in a continuous passive motion device, with pain at the pin sites determining the maximum degree of flexion; on average, 25º flexion and full extension was reached. The monotubes were replaced and sufficient distraction was confirmed by X-ray examination and adjusted if needed. After 2 months, the tubes and pins were surgically removed. After both surgeries, patients were treated with paracetamol and non-steroidal anti-inflammatory drugs as needed.
Follow-up	**2 years**
Conflict of interest/source of funding	This study was funded by the Dutch Arthritis Association. One of the authors is co-owner and CEO of Chrondrometrics GmbH.

Analysis

Follow-up issues:

- Patients visited the outpatient clinic twice before treatment and after 3 and 6 months, and subsequently every 6 months post-treatment.

Study design issues:

- Patients had been referred from peripheral hospitals for a second opinion because the patient refused the indicated total knee replacement for personal reasons mostly related to young age.
- 23 patients were originally selected and 3 were excluded: 1 based on bilateral OA; 1 because of remaining metal in the knee after anterior cruciate ligament reconstruction; and 1 withdrew the informed consent directly after treatment.
- Non-parametric statistics (two-sided paired test) were used for all parameters, to evaluate whether the follow-up values significantly differed from the baseline values. Double baseline values were averaged. Spearman correlation coefficients and unpaired non-parametric comparison of dichotomised data were used to relate/compare longitudinal changes over 2 years for different outcome parameters.
- There were no missing data.
- The 1-year follow-up results were reported in a previous paper, Intema 2011 (see Appendix A), but the findings reported for the minimum and mean joint space width in the MAC differ between the 2 papers.

Study population issues:

- Patients had predominantly medial compartmental OA (18/20) [most affected compartment was medial], stable joints (despite 3 previous anterior cruciate ligament ruptures), and an average Kellgren-Lawrence grade of 3.

Other issues: None.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **20**

WOMAC index

	% of improvement from baseline
At 1-year follow-up	70% (95%CI 38.6 to 152.5%)
At 2-year follow-up	74% (95%CI 45.8 to 161.6%)

- Both improvements from baseline were significant (p<0.001).
- The individual components of the WOMAC score (pain, stiffness and function) all improved significantly (all p<0.005 at each time point) in a similar manner.

VAS pain score improvement

	% of decrease in VAS* pain score from baseline
At 1-year follow-up	-58% (95%CI -73.8 to -39.3%)
At 2-year follow-up	-61% (95%CI -78.3 to -39.3%)

*VAS pain score measured on a 10-point visual analogue scale, with a higher score indicating more severe pain.

- Both improvements from baseline were significant (p<0.001).

Response to treatment

- 75% (15/20) of patients were responders (defined as an increase of more than 50% in WOMAC pain **or** function with more than 20 points of improvement in either category; or an increase of more than 20% in WOMAC pain **and** function with 10 points improvement in each category).
- 50% (10/20) of patients at 1-year follow-up and 45% (9/20) of patients at 2-year follow-up had an increase of more than 50% in WOMAC pain **and** function, with at least 20 points of improvement for both categories.

Cartilage thickness (MRI)

	Difference in mean cartilage thickness for the total subchondral bone area of the most affected compartment from baseline
At 1-year follow-up	0.6 mm (95%CI, 0.24 to 1.22)
At 2-year follow-up	0.4 mm (95%CI, 0.06 to 0.83) [from 2.35 mm to 2.78 mm]

Both improvements from baseline were significant (p=0.002 and p=0.030 for 1- and 2-year follow-up respectively).

Denuded area of subchondral bone (MRI)

	% of denuded subchondral bone area in the most affected compartment
Baseline	22% (95% CI, 12.5 to 31.5)
At 1-year follow-up	5% (95% CI, 0.4 to 8.6)
At 2-year follow-up	8% (95% CI, 3.6 to 12.2)

- Both differences from baseline were significant (p=0.001 and p=0.004 for 1- and 2-year follow-up respectively).
- No significant differences in percentage of denuded subchondral bone area were identified between 1- and 2-year follow-ups.
- The mean cartilage thickness over cartilaginous area of subchondral bone did

Safety

Complications

	% of patients (n=20)	Other
Pin tract infections	85% (17/20)	All the infections were treated by oral antibiotics (flucloxacillin) (no further details reported).
Pulmonary embolism (no DVT diagnosed in this case series)	10% (2/20)	The patients were treated by oral anticoagulants for 6 months.

Limited flexion	All patients	Limited flexion was observed directly after treatment (mean -31.6º of flexion, [95%CI -43.9 to -19.2]). Patients recovered to acceptable levels (mean -7.2º of flexion, [-15.2 to 1.1]) within 6 months, and flexion range fully normalised within 1-year follow-up (mean +2.9º of flexion, (-3.3 to 9.1)).

not change over time.

- In the least affected compartments, no clear changes in cartilage structure were observed and no significant changes at 1- and 2-year follow-up were found compared to baseline.

Joint space width (JSW) [X-ray]

	Difference in the minimum JSW in the most affected compartment from baseline
At 1-year follow-up	51% (0.55 mm, 95%CI 0.09 to 1.02; p= 0.03)
At 2-year follow-up	59% (0.57 mm, 95% CI 0.09 to 1.06; p=0.03)
	Difference in mean JSW in the most affected compartment from baseline
At 1-year follow-up	24% (0.66 mm, 95% CI 0.06 to 1.26; p= 0.03)
At 2-year follow-up	21% (0.36 mm, 95% CI 0.13 to 0.85; p=0.11)

Collagen type II synthesis marker PIIANP

	Concentration of collagen type II synthesis marker PIIANP (ng/ml)	% difference
At 6-month follow-up	1811 (95%CI, 1645 to 1977)	
At 2-year follow-up	1856 (95% CI, 1642 to 2071)	+3% (95% CI, -8 to 18%) p=0.69

Collagen type II breakdown marker CTXII

	Concentration of collagen type II breakdown marker CTXII (ng/mmol creat)	% difference
At 6-month follow-up	329 (95% CI, 249 to 410)	
At 2-year follow-up	229 (95%CI ,188 to 269)	-31% (-37 to -1%) **p=0.006**

Ratio PIIANP/CTXII

- + 25% (95% CI, 18 to 103) (from 7.5 [5.2-9.9] to 9.4 [7.7-11.1] at 2-year follow-up.
- p= 0.07

Primary structural outcome parameters of the whole joint (all compartments)

	Baseline	**1 year**	**2 years**	**p< (0-1)**	**p< (0-2)**	**p< (1-2)**
ThCtAB (mm)	3.3 (3.1-3.4)	3.6 (3.4-3.8)	3.5 (3.3-3.7)	**0.005**	**0.040**	0.212
dABp (%)	11.3 (6.6-16.0)	2.5 (0.4-4.6)	4.3 (2.0-6.6)	**0.001**	**0.002**	0.064
ThCcAB (mm)	3.6 (3.4-3.8)	3.7 (3.5-3.9)	3.6 (3.4-3.8)	0.470	0.590	0.350
VC (mm3)	3018 (2669-3368)	3316 (2899-3732)	3263 (2845-3680)	0.100	**0.020**	0.232
JSW (mm)	4.8 (4.3-5.3)	5.2 (4.7-5.7)	5.3 (4.4-5.8)	0.057	0.053	0.809

Abbreviations used: CI, confidence interval; dABp, percentage of denuded subchondral bone area; JSW, joint space width; MRI, magnetic resonance imaging; OA, osteoarthritis; ThCcAB, cartilage thickness over cartilaginous area of subchondral bone; ThCtAB, cartilage thickness over total subchondral bone area; VAS, visual analogue scale; VC, cartilage volume; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

Study 3 Deie M (2010)

Details

Study type	**Case series**
Country	Japan
Recruitment period	2002-2005
Study population and number	n=**6** patients with knee OA
Age and sex	Mean 49 years; 67% (4/6) female
Patient selection criteria	Patients with grade 3 or greater osteoarthritis using the Kellgren-Lawrence classification, at 1 or 2 compartments of the tibiofemoral joint.
Technique	The distraction arthroplasty was done under lumbar or general anaesthesia. Before the distraction, arthroscopy was used and when meniscal tears were found, a partial meniscectomy was done. Bone marrow stimulation was then performed. The OA lesions were either drilled or microfractured before the external distraction device was fixed. A soft knee brace was fixed for 2 weeks. Continuous passive motion exercise started 2 weeks after the procedure and continued for about 2 weeks. Patients could walk with partial weight bearing from 3 weeks after the procedure and with full weight bearing 1 month after the procedure. The external fixation device was removed 2-3 months after the procedure. The fixation period of the distraction device was mean 9 weeks.
Follow-up	**Mean 3 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: None
Study design issues:

- Distraction arthroplasty was originally done on 7 patients but 1 patient was excluded from the analysis because he was diagnosed with rheumatoid arthritis after the procedure.
- Preoperative and postoperative data were analysed using the paired t test.

Study population issues:

- Patient population consisted of 1 Kellgren-Lawrence grade 3 and 5 grade 4.

Other issues: None

Key efficacy and safety findings

Efficacy

Number of patients analysed: **6**

- The follow-up arthroscopies showed that the regions treated with the bone marrow-stimulation procedure were covered with newly formed tissues in all patients.

Japan orthopaedic association score (JOA)*

	Before the procedure (timing not reported)	At the latest follow-up (mean 3 years)	p value
JOA score (mean [range]) (points)	56 (55-60)	81 (70-85)	**p<0.001**

***** The JOA score measures 4 domains (pain on walking, pain on ascending or descending stairs, range of motion, and joint effusion) totalling a maximum of 100 points, with higher scores indicating better function.

Range of motion (ROM)

	Before the procedure (timing not reported)	At final follow-up (mean 3 years)	p value
ROM (mean±standard deviation) [degrees]	-5±4 to 111±5	-5±3 to 122±5	NR

Joint space*

	Before the procedure (timing not reported)	At external fixation (timing not reported)	At final follow-up (mean 3 years)
Joint space (mean [range]) (mm)	0.4 (0-1)	1.6 (0-3)	1.6 (0-3)

*Measured by the Rosenberg X-ray view

VAS pain score improvement

	Before the procedure (timing not reported)	At final follow-up (mean 3 years)	p value
VAS pain* (mean [range])	9 (8-10)	4 (1-7)	**0.001**

*VAS pain score measured on a 10-point visual analogue scale, with a higher score indicating more severe pain.

Safety

2 patients had a **superficial skin infection** around the insertion of the pin at the tibia and the femur.

Abbreviations used: JOA, Japan orthopaedic association; NR, not reported; OA, osteoarthritis; ROM, range of motion; VAS, visual analogue scale

Efficacy

Improvement in osteoarthritis symptoms

A case series of 20 patients with end-stage knee osteoarthritis treated by joint distraction reported significant improvements in WOMAC scores (range from 0 to 96, with lower scores indicating better outcomes) of 70% (95% confidence interval [CI] 38.6 to 152.5%) at 1-year follow-up and of 74% (95% CI 45.8 to 161.6%) at 2-year follow-up ($p<0.001$ for both improvements from baseline). The individual components of the WOMAC score (pain, stiffness and function) all improved significantly compared against baseline ($p<0.005$ for all 3 subscales at each time point: 3, 6, 12, 18 and 24 months)[2].

A case series of 6 patients with knee osteoarthritis treated by joint distraction reported a significant increase in the mean Japan orthopaedic association score (range from 0 to 100, with higher scores indicating better function) from 56 (range 55-60) before the procedure to 81 (range 70-85) at the latest follow-up (mean 3-year follow-up, $p<0.001$)[3].

Improvement in pain

A non-randomised comparative study of 61 patients treated by joint distraction and debridement (n=19) or debridement alone (n=42) reported a significant improvement in pain (measured on a 4-point Likert scale, with a higher score indicating more severe pain) within the joint distraction group, with none of the patients having no pain before the procedure and 58% (11/19) of patients having no pain 3-5 years after the procedure ($p<0.004$). In the debridement-only group, none of the patients had no pain before the procedure and 50% (21/42) of patients had no pain 3-5 years after the procedure ($p=0.163$)[1].

The case series of 20 patients reported a significant decrease in pain scores (measured on a 10-point visual analogue scale, with a higher score indicating more severe pain) of -58% (95% CI -73.8 to -39.3%) at 1-year follow-up and of -61% (95% CI -78.3 to -39.3%) at 2-year follow-up (both improvements from baseline were significant, $p<0.001$)[2].

The case series of 6 patients with knee osteoarthritis reported a significant decrease in visual analogue scale pain scores from mean 9 (range 8-10) to mean 4 (range 1-7) at final follow-up ($p=0.001$)[3].

Limb function and mobility

The non-randomised comparative study of 61 patients treated by joint distraction and debridement or debridement alone reported a significant increase in walking capacity in the joint distraction group from 10-35 minutes before the procedure to 32-51 minutes 3-5 years after the procedure ($p<0.001$). In the debridement-only

group, the walking capacity range was 12-23 minutes before the procedure and 20-31 minutes 3-5 years after the procedure (p=0.142)[1].

The non-randomised comparative study of 61 patients treated by joint distraction and debridement or debridement alone reported a significant improvement in stair climbing in both groups. In the joint distraction group, none of the patients (0/19) had no difficulty in ascending or descending stairs before the procedure and 74% (14/19) of patients had no difficulty in stair climbing 3–5 years after the procedure (p<0.002). In the debridement-only group, 33% (13/42) of patients had no difficulty in stair climbing before the procedure and 67% (28/42) of patients had no difficulty in stair climbing 3–5 years after the procedure (p<0.001)[1].

The non-randomised comparative study of 61 patients treated by joint distraction and debridement or debridement alone reported active knee flexion ranges in the joint distraction group of 75-95º before the procedure and of 110-135º 3-5 years after the procedure (p=0.029); in the debridement-only group, active knee flexion ranges were 80-110º before the procedure and 100-110º 3-5 years after the procedure (p=0.153). Passive knee flexion ranges in the joint distraction group were 85-120º before the procedure and 150-170º3-5 years after the procedure (p=0.193); in the debridement-only group, passive knee flexion ranges were 80-120º before the procedure and 90-130º3-5 years after the procedure (p=0.142)[1].

The case series of 6 patients with knee osteoarthritis reported a mean range of motion of -5º±4º to 111º±5º before the procedure and of -5º±3º to 122º±5º at final follow-up (p value not reported)[3].

Tibiofemoral angle

The non-randomised comparative study of 61 patients treated by joint distraction and debridement or debridement alone reported tibiofemoral angle ranges in the joint distraction group of 173-189º before the procedure and of 171-174º 3-5 years after the procedure (p<0.001); in the debridement-only group, the tibiofemoral angle ranges were 170-185º before the procedure and no change was observed at the end of the follow-up period[1].

Response to treatment

The case series of 20 patients reported that 75% (15/20) of patients were responders (defined as an increase of more than 50% in WOMAC pain **or** function with more than 20 points of improvement in either category; or an increase of more than 20% in WOMAC pain **and** function with 10 points improvement in each category). After 1 year, 50% (10/20) of patients and 45% (9/20) of patients at 2-year follow-up had an increase of more than 50% in WOMAC pain **and** function, with at least 20 points of improvement for both categories[2].

Increase of cartilage thickness

The case series of 20 patients reported a significant difference in mean cartilage thickness for the total subchondral bone area of the most affected compartment from baseline of 0.6 mm (95% CI 0.24 mm to 1.22 mm) at 1-year follow-up (p=0.002) and of 0.4 mm (95% CI 0.06 mm to 0.83 mm) at 2-year follow-up (p=0.03) (no further details reported)[2].

MRI evidence of cartilage regeneration

The case series of 20 patients with end-stage knee osteoarthritis reported a percentage of denuded subchondral bone area in the most affected compartment at baseline of 22% (95% CI 12.5 to 31.5%) and of 8% (95% CI 3.6 to 12.2%) at 2-year follow-up (p value compared against baseline, p=0.004)[2].

Increase in joint space width

The non-randomised comparative study of 61 patients treated by joint distraction and debridement or debridement alone reported mean joint spaces on X-ray in the joint distraction group of 2.5 mm before the procedure and of 4.3 mm 3-5 years after the procedure (p<0.001); in the debridement-only group, mean joint spaces were 2.7 mm before the procedure and 2.4 mm 3-5 years after the procedure (p=0.135)[1].

The case series of 20 patients reported a significant difference in the minimum joint space width in the most affected compartment from baseline of 59% (0.57 mm, 95% CI 0.09 mm to 1.06 mm; p=0.03) after 2 years. The difference in mean joint space width in the most affected compartment from baseline was 21% (0.36 mm, 95% CI 0.13 mm to 0.85 mm; p=0.11) after 2 years[2].

The case series of 6 patients with knee osteoarthritis reported mean joint spaces (measured by the Rosenberg X-ray view) of 0.4 mm (range 0-1 mm) before the procedure and of 1.6 mm (range 0-3 mm) at final follow-up[3].

Safety

Thromboembolic events

Deep vein thrombosis was reported in 11% (2/19) of patients treated by joint distraction in a non-randomised comparative study of 61 patients treated by joint distraction and debridement (n=19) or debridement alone (n=42); in 1 patient the thrombosis resolved after heparinisation and 1 patient developed a non-fatal pulmonary embolism (no further details provided)[1].

Pulmonary embolism was reported in 10% (2/20) of patients in a case series of 20 patients with end-stage knee osteoarthritis; both patients were treated by oral anticoagulants for 6 months (no further details provided)[2].

Infection

Pin track infections were reported in 18% of patients (absolute number not given) treated by knee joint distraction in the non-randomised comparative study of 61 patients treated by joint distraction and debridement (n=19) or debridement alone (n=42); all patients responded completely to local cleaning and systemic antibiotics (no further details provided)[1].

Pin track infections were reported in 85% (17/20) of patients treated by knee joint distraction in the case series of 20 patients; all the infections were treated by oral antibiotics (flucloxacillin; no further details provided)[2].

Superficial skin infections around the insertion of the pin were reported in 33% (2/6) of patients treated by knee joint distraction in a case series of 6 patients with knee osteoarthritis (no further details provided)[3].

Stiffness

Limited flexion immediately after treatment was reported in all patients (20/20) in the case series of 20 patients (mean -31.6º of flexion, 95% confidence interval [CI] -43.9º to -19.2º). Flexion improved at 6 months (mean -7.2º of flexion, CI -15.2º to 1.1º) and flexion range fully normalised within 1 year (mean +2.9º of flexion (-3.3º to 9.1º)[2].

Validity and generalisability of the studies

- Limitations of the evidence base: lack of randomised and comparative studies; small number of patients included in the studies.
- Only 3 studies are included in the overview.
- The follow-up length ranges between 2 and 5 years.
- The studies did not assess quality of life or patient satisfaction.

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

- Mosaicplasty for knee cartilage defects. NICE interventional procedure guidance 162 (2006). Available from http://www.nice.org.uk/guidance/IPG162
- Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis. NICE interventional procedure guidance 230 (2007). Available from http://www.nice.org.uk/guidance/IPG230
- Individually magnetic resonance imaging-designed unicompartmental interpositional implant insertion for osteoarthritis of the knee. NICE interventional procedure guidance 317 (2009). Available from http://www.nice.org.uk/guidance/IPG317
- Mini-incision surgery for total knee replacement. NICE interventional procedure guidance 345 (2010). Available from http://www.nice.org.uk/guidance/IPG345
- Platelet-rich plasma injections for osteoarthritis of the knee. NICE interventional procedure guidance 491 (2014). Available from http://www.nice.org.uk/guidance/IPG491
- Arthroscopic radiofrequency chondroplasty for discrete chondral defects of the knee. NICE interventional procedure guidance 493 (2014). Available from http://www.nice.org.uk/guidance/IPG493

Technology appraisals

- The use of autologous chondrocyte implantation for the treatment of cartilage defects in the knee joints. NICE technology appraisal 89 (2005). Available from http://www.nice.org.uk/guidance/TA89

Clinical guidelines

- Osteoarthritis: Care and management in adults. NICE clinical guideline 177 (2014). Available from http://www.nice.org.uk/guidance/CG177

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 is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Specialist Advisor Questionnaires for joint distraction for knee osteoarthritis without alignment correction were submitted and can be found on the NICE website [INSERT HYPER LINK TO MAIN IP PAGE].

Patient commentators' opinions

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

Issues for consideration by IPAC

- No ongoing trials.

References

1. Aly TA, Hafez K, and Amin O (2011) Arthrodiatasis for management of knee osteoarthritis. Orthopedics.34 (8) e338-e343.
2. Wiegant K, Van Roermund PM, Intema F et al. (2013) Sustained clinical and structural benefit after joint distraction in the treatment of severe knee osteoarthritis. Osteoarthritis and Cartilage.21 (11) 1660-1667.
3. Deie M, Ochi M, Nakamae A et al. (2010) Knee articulated distraction arthroplasty for the middle-aged osteoarthritic knee joint. Techniques in Knee Surgery.9 (2) 80-84.

Appendix A: Additional papers on joint distraction for knee osteoarthritis without alignment correction

The following table outlines the studies that are considered potentially relevant to the IP 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
Abouheif MM. (2010) Repair of a large osteochondral defect in the knee joint using autologous and artificial bone graft combined with motion preserving distraction arthroplasty: a case report. Arch Orthop Trauma Surg.130, 231-236.	Case report n=1 Follow-up=4.5 years	Satisfactory short- and mid-term result, with a painless, stable knee joint with a good functional range of motion.	Single case report with no numerical results.
Deie M, Ochi M, Adachi N et al. (2007) A New Articulated Distraction Arthroplasty Device for Treatment of the Osteoarthritic Knee Joint: A Preliminary Report. Arthroscopy - Journal of Arthroscopic and Related Surgery.23 (8) 833-838.	Case series n=6 Follow-up=1-3.5 years	The Japanese Orthopaedic Association knee score, range of motion, and joint space values were significantly improved in all cases at the latest follow-up ($p < 0.05$). Scores on a visual analogue pain scale were also significantly improved ($p < 0.05$).	Same study population and same results as in Deie 2010 study (which is included in Table 2).
Intema F, Van Roermund PM, Marijnissen ACA et al. (2011) Tissue structure modification in knee osteoarthritis by use of joint distraction: An open 1-year pilot study. Annals of the Rheumatic Diseases.70 (8) 1441-1446.	Case series n=20 Follow-up=1 year	• Radiography demonstrated an increase in mean and minimum JSW (2.7 to 3.6 mm and 1.0 to 1.9 mm; $p<0.05$ and <0.01). • MRI revealed an increase in cartilage thickness (2.4 to 3.0 mm; $p<0.001$) and a decrease of denuded bone areas (22% to 5%; $p<0.001$). • Collagen type II levels showed a trend towards increased synthesis (+103%; $p<0.06$) and decreased breakdown (-11%; $p<0.08$). • The WOMAC index increased from 45 to 77 points. • VAS pain decreased from 73 to 31 mm (both $p<0.001$).	Same study population as in Wiegant 2013 study (which is included in Table 2) but follow-up of 1 year only (while follow-up in Wiegant study is 2 years).
Mastbergen SC, Saris DBF, and Lafeber FPJG. (2013) Functional articular cartilage repair: Here, near, or is the best approach not yet clear? Nature Reviews Rheumatology.9 (5) 277-290.	Review	Joint distraction techniques have now demonstrated the capacity to stimulate actual intrinsic tissue repair. Although this progress is promising, true biological joint reconstruction remains distant on the developmental pathway of 'regenerative medicine'.	Narrative review.

Appendix B: Related NICE guidance for joint distraction for knee osteoarthritis without alignment correction

Guidance	Recommendations
Interventional procedures	**Mosaicplasty for knee cartilage defects. NICE interventional procedure guidance 162 (2006).** 1.1 Current evidence suggests that there are no major safety concerns associated with mosaicplasty for knee cartilage defects. There is some evidence of short-term efficacy, but data on long-term efficacy are inadequate. In view of the uncertainties about the efficacy of the procedure, it should not be used without special arrangements for consent and audit or research. 1.2 Clinicians wishing to undertake mosaicplasty for knee cartilage defects should take the following actions. •Inform the clinical governance leads in their Trusts. •Ensure that patients understand the uncertainty about the procedure's efficacy and the options for alternative treatments. They should provide them with clear written information. In addition, use of the Institute's information for the public is recommended. •Audit and review clinical outcomes of all patients having mosaicplasty for knee cartilage defects. The Institute may review the procedure upon publication of further evidence. **Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis. NICE interventional procedure 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 procedure 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. **Mini-incision surgery for total knee replacement. NICE interventional procedure guidance 345 (2010).** 1.1 Current evidence on the safety and efficacy of mini-incision surgery for total knee replacement is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 Mini-incision surgery for total knee replacement should only be carried out by surgeons with specific training in the procedure. 1.3 Surgeons should submit details on all patients undergoing mini-incision surgery for total knee replacement to the National Joint Registry. **Platelet-rich plasma injections for osteoarthritis of the knee. NICE interventional procedure guidance 491 (2014).** 1.1 Current evidence on platelet-rich plasma injections for osteoarthritis of the knee raises no major safety concerns; however, the evidence on efficacy is inadequate in quality. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake platelet-rich plasma injections for osteoarthritis of the knee should take the following actions. • Inform the clinical governance leads in their NHS trusts. • Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended. • Audit and review clinical outcomes of all patients having platelet-rich plasma injections for osteoarthritis of the knee (see section 7.1). 1.3 Further research into platelet-rich plasma injections for treating osteoarthritis of the knee should clearly describe patient selection and should take the form of well-designed,

	controlled studies that compare the procedure against other methods of management. Outcomes should include measures of knee function, patient-reported outcome measures and the timing of subsequent interventions. Studies aimed at assessing possible cartilage repair after platelet-rich plasma injections should include detailed radiographic or MRI imaging before and after the procedure. **Arthroscopic radiofrequency chondroplasty for discrete chondral defects of the knee. NICE interventional procedure guidance 493 (2014).** 1.1 Evidence on the efficacy of arthroscopic radiofrequency chondroplasty for discrete chondral defects of the knee is limited but shows benefit in the short term, and there are no major safety concerns. Therefore this procedure may be used with normal arrangements for clinical governance, consent and audit. 1.2 The procedure should only be carried out by clinicians with specific training in the use of arthroscopic radiofrequency ablation and with particular attention to the avoidance of thermal injury. 1.3 Further research into arthroscopic radiofrequency chondroplasty of the knee should clearly document patient selection and the types of chondral defects being treated. More evidence on long-term outcomes would be useful. **Implantation of a shock or load absorber for mild to moderate symptomatic medial knee osteoarthritis. NICE interventional procedure guidance 512 (2015)** 1.1 Current evidence on the safety and efficacy of implantation of a shock or load absorber for mild to moderate symptomatic medial knee osteoarthritis is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research. 1.2 Further research into implantation of a shock or load absorber for mild to moderate symptomatic medial knee osteoarthritis should include comparative studies against existing forms of management. Studies should record patient selection, functional outcomes, quality of life and complications. They should also report the nature and timing of any further surgery on the knee and the effect of removing the device. A minimum follow‑up period of 2–3 years is needed. NICE may update the guidance on publication of further evidence.

Technology appraisals	**The use of autologous chondrocyte implantation for the treatment of cartilage defects in the knee joints. NICE technology appraisal 89 (2005).** 1.1 Autologous chondrocyte implantation (ACI) is not recommended for the treatment of articular cartilage defects of the knee joint except in the context of ongoing or new clinical studies that are designed to generate robust and relevant outcome data, including the measurement of health-related quality of life and long-term follow-up. Patients should be fully informed of the uncertainties about the long-term effectiveness and the potential adverse effects of this procedure.
Clinical guidelines	**Osteoarthritis: Care and management in adults. NICE clinical guideline 177 (2014).** 1.4 Non-pharmacological management **Exercise and manual therapy** 1.4.1 Advise people with osteoarthritis to exercise as a core treatment (see recommendation 1.2.5), irrespective of age, comorbidity, pain severity or disability. Exercise should include: • local muscle strengthening **and** • general aerobic fitness. It has not been specified whether exercise should be provided by the NHS or whether the healthcare professional should provide advice and encouragement to the person to obtain and carry out the intervention themselves. Exercise has been found to be beneficial but the clinician needs to make a judgement in each case on how to effectively ensure participation. This will depend upon the person's individual needs, circumstances and self-motivation, and the availability of local facilities. **[2008]** 1.4.2 Manipulation and stretching should be considered as an adjunct to core treatments, particularly for osteoarthritis of the hip. **[2008]** **Weight loss** 1.4.3 Offer interventions to achieve weight loss[1] as a core treatment (see recommendation 1.2.5) for people who are obese or overweight. **[2008]** **Electrotherapy** 1.4.4 Healthcare professionals should consider the use of transcutaneous electrical nerve stimulation (TENS)[2] as an adjunct to core treatments for pain relief. **[2008]** **Nutraceuticals** 1.4.5 Do not offer glucosamine or chondroitin products for the management of osteoarthritis. **[2014]**

	Acupuncture 1.4.6 Do not offer acupuncture for the management of osteoarthritis. **[2014]** **Aids and devices** 1.4.7 Offer advice on appropriate footwear (including shock-absorbing properties) as part of core treatments (see recommendation 1.2.5) for people with lower limb osteoarthritis.**[2008]** 1.4.8 People with osteoarthritis who have biomechanical joint pain or instability should be considered for assessment for bracing/joint supports/insoles as an adjunct to their core treatments. **[2008]** 1.4.9 Assistive devices (for example, walking sticks and tap turners) should be considered as adjuncts to core treatments for people with osteoarthritis who have specific problems with activities of daily living. If needed, seek expert advice in this context (for example, from occupational therapists or Disability Equipment Assessment Centres). **[2008]** **Invasive treatments for knee osteoarthritis** 1.4.10 Do not refer for arthroscopic lavage and debridement as part of treatment for osteoarthritis, unless the person has knee osteoarthritis with a clear history of mechanical locking (as opposed to morning joint stiffness, 'giving way' or X-ray evidence of loose bodies). **[2008, amended 2014]** 1.6 Referral for consideration of joint surgery 1.6.1 Clinicians with responsibility for referring a person with osteoarthritis for consideration of joint surgery should ensure that the person has been offered at least the core (non-surgical) treatment options (see recommendation 1.2.5). **[2008]** 1.6.2 Base decisions on referral thresholds on discussions between patient representatives, referring clinicians and surgeons, rather than using scoring tools for prioritisation. **[2008, amended 2014]** 1.6.3 Consider referral for joint surgery for people with osteoarthritis who experience joint symptoms (pain, stiffness and reduced function) that have a substantial impact on their quality of life and are refractory to non-surgical treatment. **[2008, amended 2014]** 1.6.4 Refer for consideration of joint surgery before there is prolonged and established functional limitation and severe pain. **[2008, amended 2014]** 1.6.5 Patient-specific factors (including age, sex, smoking, obesity and comorbidities) should not be barriers to referral for joint surgery. **[2008, amended 2014]** 1.6.6 When discussing the possibility of joint surgery, check that the person has been offered at least the core treatments

	for osteoarthritis (see recommendation 1.2.5), and give them information about: • the benefits and risks of surgery and the potential consequences of not having surgery • recovery and rehabilitation after surgery • how having a prosthesis might affect them • how care pathways are organised in their local area. **[new 2014]**

Appendix C: Literature search for joint distraction for knee osteoarthritis without alignment correction

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	02/12/14	Issue 12 of 12, December 2014
Database of Abstracts of Reviews of Effects – DARE (Cochrane Library)	02/12/14	Issue 12 of 12, December 2014
HTA database (Cochrane Library)	02/12/14	Issue 12 of 12, December 2014
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	02/12/14	Issue 12 of 12, December 2014
MEDLINE (Ovid)	02/12/14	1946 to November Week 3 2014
MEDLINE In-Process (Ovid)	02/12/14	December 01, 2014
EMBASE (Ovid)	02/12/14	1974 to 2014 Week 48
PubMed	02/12/14	-
BLIC	02/12/14	-

Trial sources searched October 2014

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- WHO International Clinical Trials Registry

Websites searched October 2014

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Osteoarthritis, Knee/
2	((Knee or Patell*) adj4 (osteoarthrit* or cartilag* or degenerat* or detoriat*)).tw.
3	Gonarthrosis.tw. (859)
4	((degenerativ* or knee*) adj4 arthrit*).tw.
5	QA.tw.
6	or/1-5
7	Arthrodiatas*.tw.
8	((Realign* or re-align*) adj4 osteotom*).tw.
9	((Joint or bone*) adj4 (distract* or seperat* or pull* or move* or apart* or align* or realign* or re-lign*)).tw.
10	KJD.tw.
11	ilizarov technique/ or osteogenesis, distraction/ (
12	((osteogensis* or call* or callotas* or osteodistract*) adj4 Distract*).tw.
13	(ilizarov* adj4 (techni* or method* or apparat* or fix* or frame*)).tw.
14	or/7-13
15	6 and 14
16	Animals/ not Humans/
17	15 not 16