NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of joint distraction for ankle osteoarthritis

Osteoarthritis of the ankle is caused by deterioration of the cartilage and underlying bone in the ankle joint, resulting in stiffness, swelling, pain and difficulty in walking. In joint distraction for ankle osteoarthritis, an operation is done to separate the bones on either side of the ankle 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 February 2015 and updated in August 2015.

Procedure name

- Joint distraction for ankle osteoarthritis

Specialist societies

- British Orthopaedic Foot & Ankle Society
- British Limb Reconstruction Society.

Description

Indications and current treatment

Osteoarthritis of the ankle is the result of progressive deterioration of the articular cartilage 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 ankle 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 arthroscopic surgery (to remove loose bodies and bone spurs and to smooth the cartilage surfaces of the ankle joint), fusion surgery or total ankle replacement.

What the procedure involves

Joint distraction for ankle osteoarthritis 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 with the aim of stimulating cartilage healing.

With the patient under spinal block or general anaesthesia, an external frame is fitted to the ankle. The frame is secured to the tibia and the foot with pins and wires. The ankle is distracted over several days, gradually increasing the distance between the cartilaginous surfaces of the joint (usually up to about 5 mm). Distraction is usually maintained for about 2–3 months before the frame is removed. During this time, the patient is able to walk. The distraction is thought to enhance continuous flow of synovial fluid through the joint and this 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.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to joint distraction for ankle osteoarthritis. The following databases were searched, covering the period from their start to 27 August 2015: 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 ankle osteoarthritis.
Intervention/test	Joint distraction.
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 about 180 patients from 2 randomised controlled trials (RCTs)[1-4] and 6 case series[3-8].

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 joint distraction for ankle osteoarthritis

Study 1 Saltzman CL (2012)

Details

Study type	**RCT**
Country	USA
Recruitment period	2002-2006
Study population and number	n=**36 (18 fixed distraction versus 18 distraction with motion)** patients with advanced ankle osteoarthritis.
Age and sex	Mean 41.5 years; 67% (24/36) male BMI: mean 29.9 kg/m^2
Patient selection criteria	Patients with symptomatic, isolated, unilateral end-stage ankle osteoarthritis
Technique	All procedures were done by 1 or 2 surgeons using the same technique. Patients were treated by an arthroscopic ankle joint lavage with removal of any extra-articular anterior osseous osteophytes before the distraction. If the anterior osteophytes were too large to remove arthroscopically, they were removed by an open incision through an extension of the arthroscopic portals. Intra-articular joint debridement was not performed. For patients in the fixed distraction group, distraction rods without hinges were use. For patients in the distraction with motion group, distraction rods with hinges were used, with an unhinged posterior rod being detached during motion therapy. During the procedure, the ankle was distracted 5 mm as measured with use of fluoroscopy. Patients in the motion group began therapy 1 week after the procedure. The fixator was removed between 85 and 95 days after application. The patient then wore a removable below-the-knee Velcro-strapped rocker-bottom boot for one month after fixator removal and began weight-bearing in the boot. The patient gradually returned to full weight-bearing without boot immobilisation by 6 months.
Follow-up	**24 months after frame removal**
Conflict of interest/source of funding	This project was funded by a research grant from the National Institutes of Health. One or more of the authors received payments or services, either directly or indirectly, from a third party in support of an aspect of this work. In addition, one or more of the authors, or his or her institution, has had a financial relationship, in the 36 months prior to submission of this work, with an entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work.

Analysis

Follow-up issues:

- 4 patients who enrolled in the study withdrew before having surgery.
- Follow-up evaluations were done at 1, 3, 6, 9 weeks after the procedure and at 1, 26, 52 and 104 weeks after fixator removal.
- In the motion group, no patients were lost to follow-up and 1 patient had conversion to an arthrodesis between the 52- and 104-week visits after fixator removal.
- In the fixed group, 1 patient dropped out before the 1-week visit post fixator removal, 1 dropped out after the 1-week visit post fixator removal, and 1 dropped out after the 52-week visit. Three additional patients underwent ankle arthrodesis, 1 before the 52-week visit and 2 between the 52-week and 104-week visits.
- Few values were missing at the 1-week visit after fixator removal due to administrative problems unrelated to the patient's condition.

Study design issues:

- Patients completed the self-assessment ankle osteoarthritis scale (AOS, higher score indicates more pain and disability) and SF-36 questionnaires at each visit.
- Patients were randomised to 1 of the 2 treatment groups with use of a randomisation schedule prepared in advance. Randomisation took place in the operating room after arthroscopic or open resection of the anterior osteophytes had been performed. Subjects were randomised in block sizes of 2 and 4, determined at random. Sealed envelopes containing the treatment assignments for sequential patients were opened and assignments were made in the operating room after osteophyte removal had been completed and the incisions had been closed.

Study population issues: None reported.
Other issues: None.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **36 (18 fixed distraction versus 18 distraction with motion)**

Conversion to arthrodesis

- Fixed group: 17% (3/18) of patients were treated by ankle arthrodesis, 1 before the 52-week visit and 2 between the 52-week and 104-week visits.
- Motion group: 6% (1/18) of patients had conversion to an arthrodesis between the 52-week and 104-week visits.

Combined AOS score (points) – longitudinal analysis (assuming data missing at random).

Time point	Fixed group	Motion group	Difference (fixed group – motion group)	p value (between group difference in means)
Pre-treatment	62.8	63.1	-0.4	0.93
1 week after fixator removal	47.7	38.0	9.7	0.21
26 weeks after fixator removal	54.2	34.6	19.5	<0.01
52 weeks after fixator removal	54.5	33.1	21.4	<0.01
104 weeks after fixator removal	48.4	27.4	21.0	<0.01

Before-after difference in mean AOS scores (score at 104 weeks versus baseline)

- Motion group: -35.8 (-57%), p<0.01
- Fixed group: -14.4 (-23%), p<0.02

Physical component summary (PCS) of the SF-36 questionnaire

The motion group showed better PCS outcomes than the fixed group at 26 weeks after fixator removal (p=0.02) and at 104 weeks after fixator removal (p=0.05) but not at 52 weeks after fixator removal (p=0.49).

Safety

- **Pin-track infections**: 43 episodes in 53% (19/36) of patients
  - All infections were treated initially with oral antibiotics (cephalexin, 250 mg 4 times daily for 7 days). Four persisted, and the pins were removed. Two of these 4 infections occurred in patients who were thought to have acute osteomyelitis and were treated to resolution with 6 weeks of intravenous antibiotics.
- Areas of **numbness** in the medial calcaneal branch of the tibial nerve and the deep peroneal distribution onto the great toe after distractor placement: 22% (8/36) of patients.
  - When numbness was identified, X-rays were made and, if distraction exceeded 5 mm, it was reduced to this level. No other treatment was given.
  - Four cases resolved with the frame on, 2 resolved within 3 months after frame removal, and 2 patients were left with residual numbness. Two years after frame removal, 1 patient had mild decreased sensation on the dorsal aspect of the hallux, and the other had mild tingling on the plantar aspect of the foot that continued to decrease.
  - With the small numbers studied, a significant association between neuropraxia and treatment group could not be identified.
- A symptomatic **deep venous thrombosis** distal to the knee was reported in 3% (1/36) of patients and was treated by anticoagulation therapy.

Abbreviations used: AOS, ankle osteoarthritis scale; BMI, body mass index; PCS, physical component summary; SD, standard deviation; SF, short form.

Study 2 Nguyen M P (2015)

Details

Study type	**Cohort follow-up of Saltzman (2012) study population.**
Country	USA
Recruitment period	2002-2006
Study population and number	n=**36 (18 fixed distraction and 18 distraction with motion)** patients with advanced ankle osteoarthritis.
Age and sex	Mean 41.5 years; 67% (24/36) male BMI: mean 29.9 kg/m^2
Patient selection criteria	Patients with symptomatic, isolated, unilateral ankle osteoarthritis with a Kellgren-Lawrence grade of 3 or 4, skeletal maturity and age no greater than 60, failure of more than a year of nonsurgical treatment, including 3 months of continuous treatment with nonsteroidal anti-inflammatory drugs and 3 months of unloading treatment, and an ability to maintain the extremity non-weight-bearing by using ambulatory aids. Exclusion criteria: inflammatory or crystal arthritis, diabetes, severe systemic illness, fibromyalgia, peripheral neuropathy, reflex sympathetic dystrophy, a previous infection of the ankle, a neuroarthropathic ankle, other symptomatic joints of the ipsilateral lower extremity, contralateral ankle osteoarthritis, ankle or hindfoot malalignment, living more than 483 km away from the hospital and current alcohol or drug abuse.
Technique	All procedures were done by 1 or 2 surgeons using the same technique. Patients were treated by an arthroscopic ankle joint lavage with removal of any extra-articular anterior osseous osteophytes before the distraction. If the anterior osteophytes were too large to remove arthroscopically, they were removed by an open incision through an extension of the arthroscopic portals. Intra-articular joint debridement was not performed. For patients in the fixed distraction group, distraction rods without hinges were use. For patients in the distraction with motion group, distraction rods with hinges were used, with an unhinged posterior rod being detached during motion therapy. During the procedure, the ankle was distracted 5 mm as measured with use of fluoroscopy. Patients in the motion group began therapy 1 week after the procedure. The fixator was removed between 85 and 95 days after application. The patient then wore a removable below-the-knee Velcro-strapped rocker-bottom boot for one month after fixator removal and began weight-bearing in the boot. The patient gradually returned to full weight-bearing without boot immobilisation by 6 months.
Follow-up	**Mean 8.3 years**
Conflict of interest/source of funding	This project was funded by a research grant from AO North America. The original study was funded by a grant from the National Institutes of Health, US department of Health & Human Services.

Analysis

Follow-up issues:

- 4 patients who enrolled in the study withdrew before having surgery.
- The primary outcome, ankle status (defined as preserved ankle joint or conversion to total ankle replacement or ankle arthrodesis) was available in 81% (29/36) patients at mean 8.3 years of follow-up; 1 patient refused to participate and 6 were lost to follow-up.
- 22 patients completed the self-assessment ankle osteoarthritis scale (AOS, higher score indicates more pain and disability) and the physical component summary (PCF) of the SF-36 questionnaire at follow-up.
- Complete AOS and SF-36 scores were available for 61% (22/36) of patients, including 5 who completed the surveys remotely without a return visit.

Study design issues: No statistical comparisons of AOS and PCF scores before distraction and at 5-10 years of follow-up were performed because of the limited number of patients with complete functional scores at 5-10 years.
Study population issues: None reported.
Other issues: None.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 29

Conversion (n=29)
• Ankle arthrodesis: 28% (8/29)
  ○ Mean age at conversion: 42±7.5 years
• Total ankle arthroplasty: 17% (5/29)
  ○ Mean age at conversion: 58±6.5 years
• Patients with native ankle joint: 55% (16/29)
Of the 13 conversions, 2 were performed within 1 year after ankle distraction, 3 in the second year, 1 in the third year, 1 in the fifth year, 3 in the sixth year, 2 in the seventh year and 1 in the eighth year.

Predictors of ankle survival at mean 8.3 years
<table>
<tr><th></th><th>HR (95% CI)</th><th>p value</th></tr>
<tr><td>Fixed distraction versus motion</td><td>0.094 (0.017-0.525)</td><td><0.01</td></tr>
<tr><td>AOS score at 2 years (42 or less versus more than 42)</td><td>0.048 (0.0028-0.84)</td><td>0.04</td></tr>
<tr><td>Improvement of AOS score at 2 years</td><td>1.75 (0.07-44.02)</td><td>0.73</td></tr>
<tr><td>Age at distraction*</td><td>0.91 (0.83-0.99)</td><td>0.04</td></tr>
</table>
*Older patients had a lower failure rate compared against those who were 1 year younger.

Mean AOS scores (at 5-10 years, n=22)
• Native ankle group: 59.8±20.7 (versus 60.7±12.2 before distraction)
• Conversion group: 42.5±35.3 (versus 59.5±12.5 before distraction)

Physical component summary (PCS) of the SF-36 questionnaire (at 5-10 years, n=22)
• Native ankle group: 32.8±9.5
• Conversion group: 37.8±11.8

Imaging findings (n=10 with native ankle)
Ankle images consistently demonstrated subchondral sclerosis, osteophyte formation and osseous deformity consistent with Kellgren-Lawrence grade-3 or 4 ankle osteoarthritis.

Final follow-up CT scans revealed some loss of the benefit seen at 2 years, with increases in cystic formation and osseous sclerosis consistent with the natural progression of osteoarthritis.
</td><td>No safety outcomes not already reported in study 1.</td></tr>
<tr><td colspan="2">Abbreviations used: AOS, ankle osteoarthritis scale; BMI, body mass index; CI, confidence interval; HR, hazard ratio; PCS, physical component summary; SD, standard deviation; SF, short form.</td></tr>
</table>

Study 3 Marijnissen ACA (2002)

Details

Study type	**Case series (prospective study) and RCT (patients were included in Marijnissen 2013)**
Country	Netherlands (cases series and RCT) and Belgium (cases series)
Recruitment period	1993-2000 (case series) and 1997-1999 (RCT)
Study population and number	n=**74** patients with severe ankle osteoarthritis (OA) • Case series: n=57 • RCT: n=17 (9 joint distraction vs 8 debridement)
Age and sex	• Case series: mean 44 years; 54% male • RCT: mean 44.5 years; 65% male
Patient selection criteria	• Case series, inclusion criteria: refractory, severe OA; exclusion criteria: intra-articular infection, OA in both ankle joints and psychological problems that would not allow a 3-month period of distraction. • RCT, inclusion criteria: scores on 3 of the 5 clinical parameters (pain, functional impairment, physical impairment, impaired joint mobility and joint space narrowing) exceeding 50% of the maximum score. Exclusion criteria: same as in the case series.
Technique	• Case series: distraction was preceded, when necessary, by arthroscopic debridement. Intra-articular fibrotic tissue and osteophytes, if present, were removed by shaving in 35 of 57 patients so that the foot could be placed in the plantigrade position that is necessary for distraction. • RCT: debridement was performed in 7 of the 9 patients in the joint distraction group and in all 8 patients in the debridement control group. No articular cartilage surgery was performed. • For both: distraction of the joint was done twice a day for 0.5 mm each until a total distraction of at least 5 mm was reached. In 2 patients in the cases series, equinus position of the foot was gradually corrected in combination with the distraction. Ankle distraction was maintained for 3 months. Full weight bearing was allowed within a week after surgery. The loss of plantar flexion in the ankle during walking was compensated by use of a sole fitted below the foot. Physical therapy and medication were administered at the patient's request only. After removal of the frame, all patients were able to walk with or without crutches.
Follow-up	• **Cases series: mean 2.8 years** • **RCT: 1 year**
Conflict of interest/source of funding	The study was supported by a grant from the Dutch Arthritis Association.

Analysis

Follow-up issues:

- Case series:
  - 11 patients had been followed up for less than 1 year and were therefore not included in the analysis.

Study design issues:

- Pain, function, clinical status, ankle joint mobility, radiographic joint space width, and subchondral sclerosis were evaluated before treatment and yearly thereafter.
- One observer who was not involved in the surgery performed the clinical examinations of all patients in the 3 hospitals.
- X-rays were evaluated by 1 blinded observer.
- The Wilcoxon signed rank test for correlated data was used to compare data obtained before and after treatment and to compare data from different time points after treatment.
- For the RCT, power analysis dictated 8 patients per group. The Mann-Whitney U test was used to evaluate if joint distraction had a better clinical result than arthroscopic debridement alone. Statistical evaluation was performed by intent-to-treat analysis for all randomised patients. The Spearman correlation was used to compare clinical outcome with radiographic parameters.

Study population issues: The values before treatment in the debridement group were not significantly different from those in the distraction groups in the RCT and in the case series.

Other issues: Patient overlap with Marijnissen (2014) and with Ploegmakers (2005) studies which are both included in table 2.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: n=74 patients with severe ankle osteoarthritis (OA)
Case series: n=57
RCT: n=17 (9 joint distraction vs 8 debridement)

Pain
• Case series
○ One year after the procedure (n=38), the average score for pain decreased by 38% (p<0.0001).
○ 23% (13/57) of patients withdrew from the study because of persistent pain. 62% (8/13) of patients withdrew within 1 year after distraction. All the patients who withdrew were treated by arthrodesis.

Percentage of treated patients showing clinically important differences in pain during follow-up
<table>
<tr><th>Follow-up</th><th>% of patients showing ≥ 35% improvement in pain</th></tr>
<tr><td>1 year (n=38)</td><td>55</td></tr>
<tr><td>2 years (n=27)</td><td>63</td></tr>
<tr><td>3 years (n=19)</td><td>58</td></tr>
<tr><td>4 years (n=10)</td><td>50</td></tr>
<tr><td>5 years (n=7)</td><td>71</td></tr>
<tr><td>6 years (n=6)</td><td>83</td></tr>
<tr><td>7 years (n=1)</td><td>100</td></tr>
</table>
The percentages of patients who showed ≥ 35% improvement in clinical parameters were calculated according to the Outcome Measures in Rheumatology Clinical Trials criteria.

• RCT
○ One year after the procedure (n=9), the average score for pain decreased from 72% to 37% of the maximum score (p<0.003).
○ In the group treated with debridement alone, 37.5 % (3/8) of patients did not reach the 1 year follow-up despite the experimental setup because of persistent severe pain. They were considered treatment failures and underwent joint distraction between 4 months and 11 months after debridement. For these 3 patients, the last evaluation before joint distraction was used to calculate the averages for the control group. The effects of joint distraction in these 3 patients were not included in the joint distraction group.
○ The 3 patients who were treated by distraction after debridement had failed had a 59% improvement in pain.

Function
• Case series
○ One year after the procedure (n=38), the average score for function increased by 69% (p<0.0001).
○ At 3 years (n=19), the average score for function increased significantly compared against the average score at 1 year: +20% (p<0.03).
</td><td>
• Case series:
○ 28% (16/57) of patients had infections at the pin sites which were effectively treated by antibiotics.
○ In 14% (8/57) of patients, the pins through the forefoot broke, probably because of excessive strain during walking. In 62.5 % (5/8) of these patients, the broken pin was removed, and in 37.5 % (3/8) of patients, the pin was replaced; local infections were prevented or treated by antibiotics.
• RCT:
○ 33% (3/9) of patients had infections at the pin sites. In 1 patient, the pin through the forefoot was replaced, and in 1 patient, the pin through the proximal tibia was replaced.
</td></tr>
</table>

Percentage of treated patients showing clinically important differences in function during follow-up

Follow-up	% of patients showing ≥ 35% improvement in function
1 year (n=38)	53
2 years (n=27)	41
3 years (n=19)	53
4 years (n=10)	70
5 years (n=7)	86
6 years (n=6)	100
7 years (n=1)	100

The percentages of patients who showed ≥35% improvement in clinical parameters were calculated according to the Outcome Measures in Rheumatology Clinical Trials criteria.

- RCT
  - One year after the procedure (n=9), the average score for function increased from 19% to 61% of the maximum score ($p<0.004$).
  - The 3 patients who were treated by distraction after debridement had failed had a 55% improvement in function.

Clinical condition

- Case series
  - One year after the procedure (n=38), the average score for clinical condition increased by 120% ($p<0.0001$).
  - At 3 years (n=19), the average score for clinical condition increased significantly compared against the average score at 1 year: +43% ($p<0.05$).

Percentage of treated patients showing clinically important differences in clinical condition during follow-up

Follow-up	% of patients showing ≥ 35% improvement in clinical condition
1 year (n=38)	55
2 years (n=27)	63
3 years (n=19)	68
4 years (n=10)	60
5 years (n=7)	71
6 years (n=6)	83
7 years (n=1)	100

The percentages of patients who showed ≥ 35% improvement in clinical parameters were calculated according to the Outcome Measures in Rheumatology Clinical Trials criteria.

- RCT
  - One year after the procedure (n=9), the average score for clinical status increased from 20% to 69% of the maximum score ($p<0.005$).
  - The 3 patients who were treated by distraction after debridement had failed had a 55% improvement in clinical condition.

Joint mobility

- Case series
  - One year after the procedure (n=38), the average score for joint mobility increased by 8% (p not significant).

Percentage of treated patients showing clinically important differences in joint mobility during follow-up

Follow-up	% of patients showing ≥ 35% improvement in joint mobility
1 year (n=38)	13
2 years (n=27)	30
3 years (n=19)	32
4 years (n=10)	10
5 years (n=7)	14
6 years (n=6)	17
7 years (n=1)	0

The percentages of patients who showed ≥ 35% improvement in clinical parameters were calculated according to the Outcome Measures in Rheumatology Clinical Trials criteria.

- RCT
  - One year after the procedure (n=9), the average score for mobility decreased from 56% to 46% of the maximum score (p value not significant).

Impairment of maximum walking distance (case series patients)

Follow-up	Score for impaired walking distance (mean±SD)	p value (versus baseline)
Before the procedure	1.46±0.18	
1 year (n=38)	0.92±0.20	<0.03
5 years (n=7)	0.00±0.00	<0.04

Joint space width

- Case series
  - This was only evaluated in patients for whom the X-ray was useful for evaluation (n=17) and who had more than 10% joint space narrowing before treatment: 12 patients at 1 year, 10 at 2 years, 7 at 3 years, 3 at 4 years, and 3 at 5 years.
  - One year after the procedure (n=12), the average joint space width increased by 17% (p<0.04).
  - At 3 years (n=7), the mean joint space width increased significantly compared against the mean width at 1 year: +10% (p<0.05).
  - In the remaining 5 patients, joint space narrowing in the affected joint before treatment was <10%. On average, these patients showed no significant change in joint space width over time.

Percentage of treated patients showing clinically important differences in joint space width during follow-up

Follow-up	% of patients showing ≥ 25% improvement in joint space width
1 year (n=12)	33
2 years (n=10)	70
3 years (n=7)	71

4 years (n=3)	67
5 years (n=3)	67

The percentages of patients who showed ≥ 25% improvement in objective parameters were calculated according to the Outcome Measures in Rheumatology Clinical Trials criteria.

Subchondral sclerosis

- Case series
  - This was only evaluated in patients in whom the X-ray was useful for evaluation (n=17) and who had increased subchondral bone density (compared against the contralateral ankle) before treatment: 10 patients at 1 year, 7 at 2 years, 5 at 3 years, 3 at 4 years, and 2 at 5 years.
  - One year after the procedure (n=10), the subchondral bone density decreased by 10% ($p<0.003$).
  - At 3 years (n=5), subchondral bone density decreased by an additional 7% compared against it at 1 year ($p>0.23$).
  - In the remaining 7 patients without measurable subchondral sclerosis before treatment, no significant decrease in bone density over time was found on average.

Percentage of treated patients showing clinically important differences in joint space width during follow-up

Follow-up	% of patients showing ≥ 25% improvement in joint space width
1 year (n=10)	33
2 years (n=7)	70
3 years (n=5)	71
4 years (n=3)	67
5 years (n=2)	67

The percentages of patients who showed ≥ 25% improvement in objective parameters were calculated according to the Outcome Measures in Rheumatology Clinical Trials criteria.

Abbreviations used: NS, not significant; OA, osteoarthritis, SD, standard deviation.

Study 4 Marijnissen ACA (2014)

Details

Study type	**Case series compiled from 2 studies: one open prospective multicentre study (same patients as in Marijnissen 2002) and one RCT (same patients as in Saltzman 2012)**
Country	Netherlands and Belgium (cases series) and USA (RCT)
Recruitment period	1993-2001 (case series) and 2003-2007 (RCT)
Study population and number	n=**111** patients with severe ankle osteoarthritis • Case series: n=75 • RCT: n=36 (18 fixed ankle distraction vs 18 joint motion permitted ankle distraction)
Age and sex	Mean 42.7 years; 60% male (all patients) • Case series: mean 43.3 years; 57% male; BMI not reported • RCT: mean 41.4 years; 67% male; mean BMI, 29.8 kg/m^2
Patient selection criteria	All patients had severe ankle OA, mostly post-traumatic and were considered for arthrodesis.
Technique	Case series: fixed ankle distraction RCT: fixed or joint motion permitted ankle distraction.
Follow-up	**Mean follow-up:** • **Cases series: 8.1 years** • **RCT: 1.9 years**
Conflict of interest/source of funding	Not reported

Analysis
Follow-up issues: None.
Study design issues:

- The aim of this study was to conduct survival and regression analyses to identify predictors of treatment failure and clinical outcomes, through analysing follow-up data from 2 previous studies: one open prospective multicentre study (same patients as in Marijnissen 2002) and one RCT (same patients as Saltzman 2012)
- Case series: all distraction procedures were done by a single surgeon in each centre.
- Pain and functional disability were evaluated at baseline and every year after the distraction using different questionnaires in the cases series and in the RCT. Both parameters were expressed as percentage of the maximum score. In the case series, the Van Valburg functional disability questionnaire and the box scale for pain were used. In the RCT, the Ankle Osteoarthritis Scale (AOS) was used.
- Pain and functional disability as endpoints were defined at 2 years since a 2-year follow-up measurement was available for almost all patients in both cohorts.
- Failures were defined as patients who underwent an arthrodesis, developed Sudeck's atrophy, had an osteotomy or a second distraction done. Failure at 2 years and failure over time during the entire follow-up period were used as endpoints.
- Survival curves with failure as end point were constructed using the Kaplan–Meier method. Survival times were censored at the time of loss to follow-up or maximum follow-up.

Study population issues:

- Mean percentages of the maximum score for pain at baseline:
  73%±13 % (case series) versus 60%±15% (RCT), p<0.0001.

Other issues: Same patients as in Saltzman (2012) and Marijnissen (2002) and some patient overlap with Ploegmakers (2005). All 3 studies are included in table 2.

Key efficacy and safety findings

Efficacy	Safety

Number of patients analysed: **111**
Case series: n=75
RCT: n=36 (18 fixed ankle distraction vs 18 joint motion permitted ankle distraction)
 	
Treatment failures
• Over a follow-up of 12 years, 44% of procedures had failed ('failure' definition above in study design issues).
• 17% of procedures failed within 2 years of joint distraction
• 37% of procedures failed within 5 years of joint distraction
• Within 2 years after ankle distraction (n=96 after 2 years): 17% (18/105) of failures
  o 5% (6/111) patients were lost to follow-up within 2 years (1 patient died 15 months after the procedure, not related to the treatment and the reason for loss to follow-up for the other 5 was unknown).
  o 83% (15/18) of patients with treatment failure were treated by arthrodesis.
  o 11% (2/18) of patients with treatment failure developed Sudeck's atrophy.
  o 5% (1/18) of patients with treatment failure were treated by osteotomy.
• Within 5 years after ankle distraction (n=48 after 5 years): 37% of failures.
• No significant difference in the percentage of failures which occurred in the first 2 years after joint distraction was found between the case series and the RCT (respectively 18% vs. 15%, p=0.647) and no significant difference was found in time to failure between the 2 study groups (p=0.637).
• The percentage of failure was different in women versus men; in women there was a 30% failure after 2 years and in men 30% failure was still not reached after 11 years. Log-rank test confirmed the statistically significant difference in failure during follow-up between men and women (p=0.001).
 	
<u>Regression Analyses</u>
 	
The following baseline variables were included in regression analyses (linear and logistic, depending on outcome variable) to identify predictors of failure, pain, and functional disability at 2 years: gender, age, pain, functional disability, clinical condition, motion permitted distraction, BMI. Results are presented as Odds Ratios (OR). Only results significant at the p<0.05 level are reported here. To examine predictors of failure <u>over time</u> cox regression analyses were undertaken, and hazard ratios reported (HR). Again only results significant at the p<0.05 level are reported here.
 	
Prediction of failure at 2 years:
  o Univariate logistic regression analysis with failure at 2 years after joint distraction as dependent variable
  ▪ Female gender: OR 4.94 (95% CI 1.6-15.2), p=0.005
  ▪ Pain at baseline: OR 1.05 (95% CI 1.0-1.1), p=0.033.
  o Multivariate logistic regression analysis with failure at 2 years after joint distraction as dependent variable
  ▪ Female gender: OR 5.42 (95% CI 1.70-17.29), p=0.004
 	
Prediction of pain at 2 years:
  o Univariate linear regression analysis with pain at 2 years after joint distraction as dependent variable
  ▪ Pain at baseline: β 0.40 (95% CI 0.08 to 0.73), p=0.015
  ▪ Functional disability at baseline: β 0.35 (95% CI 0.003 to 0.7), p=0.048
	2 of the 105 patients available for 2-year follow-up had developed **Sudeck's atrophy.**

- Motion permitted distraction: β −19.0 (95% CI -32.1 to -6.0), p=0.005

- Multivariate linear regression analysis with pain at 2 years after joint distraction as dependent variable
  - R^2=0.144
  - Motion permitted distraction: β −20.3 (95% CI -37.02 to -3.04), p=0.021

Pain (average percentage of the maximum score ± SD)

	Baseline	At last follow-up
For the patients who were still in follow-up (n=105)	67 %±15 %	38 %±24 % (2 years after ankle distraction)
For the patients whose treatment failed (n=6)	76 %±15 %	71 %±21 % (last observed scores before failure)

Prediction of functional disability at 2 years:

- Univariate linear regression analysis with functional disability at 2 years after joint distraction as dependent variable
  - Pain at baseline: β 0.38 (95% CI 0.06 to 0.7), p=0.020
  - Functional disability at baseline: β 0.38 (95% CI 0.05 to 0.7), p=0.027
- Multivariate linear regression analysis with functional disability at 2 years after joint distraction as dependent variable
  - R^2=0.128
  - Motion permitted distraction: β −21.06 (95% CI -37.89 to -4.23), p=0.015

Functional disability (average percentage of the maximum score)

	Baseline	At last follow-up
For the patients who were still in follow-up (n=105)	68 %±15 %	36 %±23 % (2 years after ankle distraction)
For the patients whose treatment failed (n=6)	67 %±13 %	71 %±18 % (last observed scores before failure)

Prediction of failure over time:

- Univariate Cox regression analysis with failure after joint distraction as dependent variable
  - Gender: HR 2.83 (95% CI 1.46-5.48), p=0.002
- Multivariate Cox regression analysis with failure after joint distraction as dependent variable
  - Gender: HR 2.86 (95% CI 1.48-5.53), p=0.002

Abbreviations used: BMI, body mass index; CI, confidence interval; HR, hazard ratio; OR, odds ratio; SD, standard deviation.

Study 5 Ploegmakers JJW (2005)

Details

Study type	**Case series**
Country	Belgium and The Netherlands
Recruitment period	1987 - 1995
Study population and number	n=**22** patients with unilateral post-traumatic ankle OA severe enough to be considered for arthrodesis
Age and sex	Mean 37 years; 64% (14/22) male
Patient selection criteria	Patients with severe unilateral post-traumatic ankle OA who underwent joint distraction between April 1987 and July 1995 at the selected hospitals.
Technique	In each centre a single surgeon performed the procedures. The procedure was done under general anaesthesia. Distraction was carried out over a distance of 5 mm (0.5 mm twice daily for 5 days), starting the day after application of the apparatus. Full weight bearing was allowed within a few days after surgery. Generally, all patients used crutches to walk with partial weight bearing on the affected ankle shortly after leaving hospital. During the subsequent weeks, the walking distance, the frequency, and amount of loading gradually increased. After 12-22 weeks, on average at 15±3 weeks after initiation of treatment, the external fixation apparatus was removed under general anaesthesia.
Follow-up	**7 years minimum**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues:

- 27 patients met the inclusion criteria, 93% (25/27) could be traced. Three patients did not complete the questionnaires in appropriate way for evaluation. Therefore, 81% (22/27) of patients treated were available for evaluation.

Study design issues:

- The pre-treatment status of patients was evaluated retrospectively using 3 different questionnaires (the Van Valburg questionnaire, the Ankle osteoarthritis scale (AOS) and a patient satisfaction questionnaire), and by survey of the patients' charts.
- Post-treatment status (at least 7 years after treatment) was evaluated using the same questionnaires and by physical examination.
- For the Van Valburg questionnaire and the AOS, results were expressed as a percentage of the maximum score. For the patient satisfaction score, results were expressed as the number of patients in each of the 5 categories (from deterioration to clear improvement) for each parameter.
- The Wilcoxon signed rank test for paired data was used to compare status parameters before and after treatment and to compare retrospectively obtained and prospectively obtained pre-treatment data. Spearman correlation was used for comparison of outcome of different questionnaires.

Study population issues:

- Causes of OA: 86% (19/22) fracture or subluxation of the ankle joint; 5% (1/22) congenital deformation; 5% (1/22) deformation after poliomyelitis; 5% (1/22) not known.

Other issues: Patient overlap with Marijnissen 2014 and with Marijnissen 2002 (both included in table 2) for 16 patients.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **22**

Treatment failure: 27% (6/22) of patients

- 83% (5/6) of patients were treated by arthrodesis; 3 within the first year after treatment and 2 four years after treatment.
- 17% (1/6) of patients suffered from an incomplete Sudeck's atrophy.

Pain (% of the maximum score, n=16)

Questionnaire	Mean ± SE pain score before joint distraction	Mean ± SE pain score at least 7 years after joint distraction	p value	Further details
Clinical evaluation	78±3%	30±5%	< 0.0001	
AOS score for pain	67±6%	25±6%	< 0.002	Score decreased in 87.5% (14/16) of patients after treatment. In 12.5% (2/16) of patients, score increased; One of these patients could only answer 1 out of the 9 questions in the questionnaire relating to the situation before treatment, making the result unreliable.

Functional ability / disability (% of the maximum score, n=16)

Questionnaire	Mean pain score before joint distraction	Mean ± SE pain score at least 7 years after joint distraction	p value	Further details
Clinical evaluation (ability)	20±4%	73±6%	< 0.001	Functional ability increased in all patients, except 1 (pre-treatment score of 60% which remained unchanged after treatment)
AOS score for disability	74±5%	32±7%	< 0.001	Disability measured by the AOS decreased after treatment in 87.5% (14/16) of patients. In 2 patients the disability score increased, and 1 of these patients also showed an increase in pain.

Total AOS score (pain and disability)

Mean total score before joint distraction: 69±4%

Mean total score at least 7 years after joint distraction: 29±6%

p< 0.001

Clinical status (%)

- Clinical evaluation (n=16)

Mean score before joint distraction: 21±7%

Safety

- **Persisting pain**: 27% (6/22) of patients
- **Sudeck's atrophy**: 5% (1/22) of patients (unclear if related to the procedure).

Mean score at least 7 years after joint distraction: 77±6%

p value< 0.001

In 1 patient, pre-treatment score was 100% and remained unchanged after joint distraction.

In 1 patient, there was a 33% decrease in their clinical status.

In 1 patient, physical examination was not recorded adequately in the chart.

Ankle mobility (measured in degrees and expressed as a % of the range of motion of the contralateral control ankle)

- Clinical evaluation (n=16)

Mean score before joint distraction: 52±7%

Mean change: 34±23%

p value> 0.39

Mobility increased in 37.5 % (6/16) of patients, decreased in 37.5% (6/16) of patients and remained unchanged in 1 patient. In 3 patients no pre-operative data were available from the patients' charts.

Patient satisfaction

	Worsened	Similar	Minimally improved	Improved	Noticeably improved
Function	7% (1/15)	13% (2/15)	20% (3/15)	7% (1/15)	53% (8/15)
Pain	6% (1/16)	13% (2/16)	6% (1/16)	19% (3/16)	56% (9/16)

Numbers refer to number of patients who replied with the respective answer to each item of the Van Valburg questionnaire when comparing the situation after joint distraction with that before treatment at time of evaluation. One patient was not able to answer each specific question with respect to function.

Abbreviations used: AOS, ankle osteoarthritis scale; OA, osteoarthritis; SE, standard error.

Study 6 Paley D (2008)

Details

Study type	**Case series**
Country	USA
Recruitment period	1992-2006
Study population and number	n=**23** patients with painful ankle OA
Age and sex	Mean 45 years (responders to the questionnaires only); 39% (9/23) male
Patient selection criteria	Patients treated by hinged ankle distraction with external fixation who had a minimum 2-year follow-up.
Technique	During the procedure, the ankle was distracted by 2 mm. The ankle was then distracted at a rate of 1 mm per day from the day after the procedure to 5 days after the procedure. The goal was to distract the ankle up to 8-10 mm. The external fixation device was maintained for 3 months. Weight bearing was allowed. The patient removed the posterior distraction rod to do daily ankle range-of-motion exercises and attended physical therapy 3 times a week.
Follow-up	**Mean 64 months (for the 18 responders)**
Conflict of interest/source of funding	The main author is a consultant for Smith & Nephew and Orthofix.

Analysis

Follow-up issues:

- The charts of 32 patients were retrospectively reviewed for the study and in 72% (23/32) of patients the charts were available for complete review, 9 male, 14 female.
- 18 patients responded to the questionnaires; 3 were found but refused to participate in the study and 11 patients could not be located.

Study design issues:

- Retrospective study.
- The procedures were done by 4 different surgeons.

Study population issues:

- Diagnoses: 87% (20/23) post-traumatic arthrosis, 4% (1/23) polio, 4% (1/23) fibular hemimila and 4% (1/23) achondroplasia.
- Adjunctive surgical procedures done together with ankle distraction: 22 anterior ankle osteophyte resections, 8 supramalleolar osteotomies, 7 lengthening of the Achilles tendon, 3 tarsal tunnel decompressions, 9 core decompressions of the talus/tibia, 6 hardware removals, 1 fasciotomy, 1 plantar fascial release, 1 proximal tibial lengthening, 2 gradual equinus corrections, 3 posterior ankle osteophyte resections and 2 hindfoot deformity corrections.
- 48 % (11/23) of patients received a series of 3 growth hormone injections (10 mg per intra-articular ankle injection) during the treatment.
- 9% (2/23) of patients had previously been treated by ankle distraction with the same protocol and opted for a second treatment. One patient had relief for 4 years and the other 1 for 2 years before reattempting distraction.

Other issues: None.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 18 (responders to the questionnaires)

Average duration of treatment with external fixation: 17 weeks.

Total arc of ankle joint motion before the procedure (mean): 28º
Total arc of ankle joint motion after the procedure (mean): 27º

Conversion to other ankle surgery
% of patients treated by another ankle procedure: 11% (2/18)
• 1 patient was treated by ankle fusion
• 1 patient was treated by ankle replacement

Foot and ankle questionnaire
At mean 64 months of follow-up,
• Mean score: 71 (range 44-98)*
• Mean score in the group with 5 years or less of follow-up (n=9): 79*
• Mean score in the group with more than 5 years of follow-up (n=9): 52*
• No significant difference for pain between the group with 5 years or less of follow-up and the group with more than 5 years of follow-up (p=0.187).
• Mean shoe comfort score: 47**
* Score from 0 to 100 (poor outcome to best possible outcome).
** Score from 0 to 100 (100= no discomfort).

Pain
• Patients taking pain killers such as NSAIDs occasionally for ankle pain: 61% (11/18) of patients
• Patients with only occasional moderate-to-mild ankle pain: 78% (14/18)

Ability to walk
• 77% of patients said they walked for pleasure
• 33% of patients said they could run
• 22% (4/18) of patients used an assistive device to walk
• 11% (2/18) of patients reported severe limitations.

Patient satisfaction
• Patients very satisfied or satisfied by the result of the procedure: 61% (11/18)
• Patients not satisfied with the outcome: 33% (6/18)
• Patients who would recommend this procedure to a friend: 71%.
</td><td>
Complications during distraction
<table>
<tr><th>Complication</th><th>Number of episodes</th></tr>
<tr><td>Incision and drainage of an external fixation pin site</td><td>1</td></tr>
<tr><td>Incision and drainage of the anterior ankle incision site</td><td>1</td></tr>
</table>
• Authors reported that “approximately 75%” of patients needed at least 1 course of antibiotics during the distraction treatment (further details not given).
</td></tr>
<tr><td colspan="2">Abbreviations used: NSAIDs, non-steroidal anti-inflammatory drugs; OA, osteoarthritis;</td></tr>
</table>

Study 7 Intema F (2011)

Details

Study type	**Case series (patients from the Saltzman 2012 study included in table 2)**
Country	USA
Recruitment period	2002-2006
Study population and number	n=**26** patients with severe post-traumatic ankle OA.
Age and sex	Mean 41 years; 65% (17/26) male
Patient selection criteria	Selection criteria: symptomatic isolated, unilateral Kellgren-Lawrence (KL) grade 3 or 4 ankle OA, skeletally mature and age ≤ 60 years, failure of non-operative treatment > 1 year, and capacity to maintain extremity non-weight-bearing using ambulatory aids. Excluded criteria: patients with history of inflammatory arthritis, the presence of other symptomatic joints on the ipsilateral lower extremity, contralateral ankle arthritis (KL grade 2–4), ankle or hindfoot malalignment, patients living greater than 300 miles away from treatment centre, current history of alcohol or drug abuse.
Technique	Same as in Saltzman (2012).
Follow-up	**24 months after frame removal**
Conflict of interest/source of funding	The study was financially supported by grants from the National Institutes of Health/ National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Analysis
Follow-up issues:
- Initially, 40 patients were included in the Saltzman study. Suitable CT scans were unavailable for 35% of patients (14/40) (5 patients withdrew, 1 fused before 1 year of follow-up, 3 CT scans had severe metal artefacts, and 5 baseline CT scans had technical errors).
- Double-contrast (systemically and intra-articular) axial CT scans were obtained at baseline (before treatment), and at 1- and 2-year follow-up after treatment to analyse joint space width and bone density.

Study design issues:
- Changes in bone density (in Hounsfield Units (HU), measured relative to baseline) were queried at over 30 000 discrete locations beneath the tibial and talar weight-bearing regions. The measurement grid covered a subchondral patch of nominally 650 mm2, with typically 4000 point measurements per surface (~0.17 mm^2/point).
- Bone density was measured at 1 mm intervals beneath the bone surface, along the surface normals and extending subchondrally up to 8 mm.
- Baseline and follow-up data for bone density at 1 to 8 mm from joint surface showed a normal distribution and parametric statistics were applied. Statistical significance in changes over time were determined using the paired samples T-test (the data at baseline and follow-up per patient served as a pair).
- Clinical data also showed normal distribution and significant improvement was determined by using the paired samples T-test. Spearman correlations of the sum of change in bone density for tibia and talus (mean change per point in high and low density areas) were used to identify significant correlations with clinical improvement (percentage change compared to baseline).

Study population issues: Same patients as in Saltzman (2012) study.
Other issues: None.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 26

Change in bone density over the area of 1 to 8 mm from the joint surface from baseline (mean ± SD)
At 1-year follow-up
• Tibia: -23±12% (p<0.001)
• Talus: -18±15% (p<0.001)
At 2-year follow-up
• Tibia: −21±12% (p<0.001)
• Talus: −16±15% (p<0.001)

Change in bone density (mean±SD in HU, 95% CI) compared against baseline for tibia and talus at 1 and 2 years of follow-up.
<table>
<tr><td></td><td></td><td colspan="2">1 year</td><td colspan="2">2 years</td></tr>
<tr><td></td><td></td><td>Mean±SD</td><td>95% CI</td><td>Mean±SD</td><td>95% CI</td></tr>
<tr><td colspan="6">1-3 mm beneath joint surface</td></tr>
<tr><td>> 400 HU at baseline</td><td>Tibia</td><td>−237±111</td><td>−288 to −186</td><td>−192±117</td><td>−244 to -139</td></tr>
<tr><td></td><td>Talus</td><td>−156±93</td><td>−194 to -188</td><td>−136±82</td><td>−171 to -101</td></tr>
<tr><td>< 400 HU at baseline</td><td>Tibia</td><td>123±108</td><td>77 to 169</td><td>180±143</td><td>116 to 244</td></tr>
<tr><td></td><td>Talus</td><td>41±111</td><td>−3 to 84</td><td>58±114</td><td>9 to 107</td></tr>
<tr><td colspan="6">4-8 mm beneath joint surface</td></tr>
<tr><td>> 400 HU at baseline</td><td>Tibia</td><td>−184±92</td><td>−226 to -141</td><td>−193±102</td><td>−239 to -147</td></tr>
<tr><td></td><td>Talus</td><td>−138±77</td><td>-170 to -107</td><td>−127±80</td><td>−161 to -93</td></tr>
<tr><td>< 100 HU at baseline</td><td>Tibia</td><td>144±133</td><td>83 to 206</td><td>153±131</td><td>94 to 212</td></tr>
<tr><td></td><td>Talus</td><td>92±100</td><td>51 to 133</td><td>78±144</td><td>17 to 140</td></tr>
</table>
AOS pain (mean±SD)
• Baseline: 60±3% of the maximum score
• At 1-year follow-up: 35±4% of the maximum score, p<0.001 versus baseline
• At 2-year follow-up: 35±5% of the maximum score, p<0.001 versus baseline

AOS disability (mean ± SD)
• Baseline: 67±2% of the maximum score
• At 1-year follow-up: 46±5% of the maximum score, p<0.001 versus baseline
• At 2-year follow-up: 36±5% of the maximum score, p<0.001 versus baseline</td><td>Not reported.</td></tr>
<tr><td colspan="2">Abbreviations used: AOS, ankle osteoarthritis scale; CI, confidence interval; CT, computerised tomography; HU, Hounsfield Units; KL, Kellgren-Lawrence; SD, standard deviation</td></tr>
</table>

Study 8 Tellisi N (2009)

Details

Study type	**Case series**
Country	USA
Recruitment period	1999-2006
Study population and number	n=**25** patients with painful ankle arthritis and significant ankle joint mobility (more than 20º)
Age and sex	Mean 43 years; 64% (16/25) male
Patient selection criteria	Inclusion criteria: patients with painful ankle arthritis and significant ankle joint mobility (more than 20º) who were recommended ankle arthrodesis treatment to relieve their pain. Exclusion criteria: patients with very limited ankle mobility and patients with severely distorted intra-articular geometry. Two weeks after the procedure, sutures were removed and X-rays were taken to measure the amount of distraction in the joint.
Technique	All procedures were done by 1 surgeon in 1 centre. All patients were treated by spinal anaesthesia. During the procedure, the ankle was distracted about 5 mm. Patients were admitted to the hospital after the procedure for pain control and 24 hours of IV antibiotics. Prophylactic oral antibiotics were started once IV antibiotics had completed and were continued for 10 days. Patients started weight bearing as tolerated immediately after the procedure. DVT prophylaxis was implemented after 24 hours and continued for 3 weeks or until patients were very mobile. Pin care (consisting of cleaning the pin sites once daily with diluted hydrogen peroxide) was started 2 days after the procedure. Patients were allowed to shower and wet the frame and wounds after 4 days. If the joint space was less than 5 mm, additional distraction was applied in order to reach 5 mm of joint space. The frame was removed after 12 weeks under sedation. After frame removal, a cam walker boot was applied and weight bearing as tolerated ambulation was encouraged. In cases of adjuvant supramalleolar osteotomy, the foot ring was removed after 12 weeks in the office if the osteotomy had not fully healed. This ended the distraction period. The remainder of the fixator was removed in the operating room when there was adequate healing at 16 weeks.
Follow-up	**Mean 30.5 months after frame removal**
Conflict of interest/source of funding	None reported.

Analysis

Follow-up issues:

- 92% (23/25) of patients had complete data.
- Patients had follow-up visits at 2, 6 and 10 weeks.

Study design issues:

- Retrospective study.

Study population issues:

- Etiology of ankle OA: post-traumatic OA for all patients.
- Patients treated by adjuvant procedures: 20% (5/25) Achilles tendon lengthening, 16 % (4/25) ankle arthroscopy, 4% (1/25) open arthrotomy, and 24% (6/25) supramalleolar tibial and distal fibular osteotomy to correct distal tibial deformity.

Other issues: None.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **23** **Conversion to ankle fusion** 9% (2/23) of patients were treated by ankle fusion. **AOFAS ankle score (mean)** The questionnaire AOFAS is composed of 9 items, distributed over 3 categories: pain, functional aspects and alignment (score 0 to 100 from worst to best outcomes). • Before the procedure: 55 (range 29 to 82) • At mean 30.5 months of follow-up: 74 (range 47 to 96) • Significant difference from baseline, p=0.005. • Individual AOFAS scores showed significant improvement in 74% (17/23) of patients, 17% (4/23) trended towards improvement and 9% (2/23) scored worse at latest follow-up. **AOFAS pain score (mean)** • Before the procedure: 15 (range 0 to 20) • At mean 30.5 months of follow-up: 31 (range 20 to 40) • Statistical test for difference between baseline and follow-up pain score not reported • 91% (21/23) of patients reported improved pain. **SF-36 scores** SF-36 scores were reported by the authors as showing “modest improvement in all components” but absolute numbers were not presented and the p value reported was p=0.23 (not significant). **Angle range of motion (mean, degrees)** None of the patients showed a loss of motion after distraction. • Before the procedure: 7 degrees dorsiflexion (range -5 to 15 degrees) and 32 degrees plantarflexion (range 15 to 50 degrees) • At mean 30.5 months follow-up: 4.3 degrees dorsiflexion (range 0 to 10 degrees) and 33 degrees plantarflexion (range 20 to 40 degrees) **Joint space width (X-rays)** In 91% (21/23) of patients, there was no difference in ankle joint space.	• Superficial pin infections: 100% (23/23) of patients These were controlled with a single course of antibiotics.
Abbreviations used: AOFAS, American Orthopaedic Foot and Ankle Society; DVT, deep vein thrombosis; IV, intravenous; SF, short form.	

Efficacy

Osteoarthritis symptoms

In a combined analysis of a case series of 57 patients treated by ankle joint distraction and a randomised controlled trial (RCT) of 17 patients treated by joint distraction (n=9) or debridement (n=8), 1 year after the procedure, the average score for clinical condition in the case series patients increased by 120% (n=38; p<0.0001). In the RCT patients the average score for clinical status increased from 20% to 69% of the maximum score (n=9; p<0.005). Three patients who were treated by distraction after debridement had failed had a 55% improvement in clinical condition from the last evaluation before joint distraction. At 3 years, the average score for clinical condition increased by 43% compared with the average score at 1 year in the case series (n=19, p<0.05)[3].

In an RCT of 36 patients treated by fixed distraction (n=18) or distraction with motion (n=18), the mean combined ankle osteoarthritis scale (AOS) scores were 62.8 in the fixed group and 63.1 in the motion group before the procedure (no difference between groups; p=0.93). At 52 weeks after fixator removal, the mean AOS scores were 54.5 in the fixed group and 33.1 in the motion group; at 104 weeks the mean AOS scores were 48.4 and 27.4 respectively (significant differences between groups; p<0.01 at 52 and 104 weeks)[1].

A case series of 22 patients treated by ankle joint distraction reported mean (± standard error) percentages of the maximum total AOS score before distraction of 69% (±4%) and 29% (±6%) at a minimum follow-up of 7 years after distraction (p<0.001)[5].

The case series of 22 patients reported mean (± standard error) scores for clinical status of 21% (±7%) before distraction and 77% (±6%) at a minimum follow-up of 7 years after distraction (p< 0.001)[5].

In a case series of 23 patients treated by joint distraction, the mean score for the Foot and Ankle questionnaire was 71 (range 44–98, from 0 to 100 with 0 indicating a poor outcome and 100 the best possible outcome) at mean 64 months of follow-up. In the group with 5 years or less of follow-up (n=9), the mean score was 79 and the score was 52 in the group with more than 5 years of follow-up (n=9)[6].

A case series of 25 patients treated by joint distraction reported mean American Orthopaedic Foot and Ankle Society (AOFAS) scores (0 to 100 from worst to best outcomes) of 55 (range 29 to 82) before the procedure and 74 (range 47 to 96) at a mean follow-up of 30.5 months (significant difference from baseline, p=0.005)[8].

Pain

In a combined analysis examining predictors of treatment failure of a case series of 75 patients treated by ankle joint distraction and the RCT of 36 patients, the

average percentage of the maximum score for pain (± standard deviation) at baseline was 67% (±15%) and 38% (±24%) at 2 years after ankle distraction for the patients still included in the study (n=105); for the patients whose treatment failed, the average percentage of the maximum score for pain was 76% (±15%) at baseline and 71% (±21%) before treatment failure (n=6)[4].

In the combined analysis of the case series of 57 patients treated by ankle joint distraction and the RCT of 17 patients treated by joint distraction (n=9) or debridement (n=8), 1 year after the procedure, the average score for pain in the case series patients decreased by 38% (n=38; p<0.0001). In the RCT, the average score for pain decreased from 72% to 37% of the maximum score (n=9; p<0.003). In the group treated with debridement alone, 37.5% (3/8) of patients did not reach the 1-year follow-up because of persistent severe pain. They were considered treatment failures and underwent joint distraction between 4 months and 11 months after debridement. The 3 patients who were treated by distraction after debridement had failed had a 59% improvement in pain from the last evaluation before joint distraction[3].

The case series of 22 patients reported mean (± standard error) percentages of the maximum score for pain measured by clinical evaluation before distraction of 78% (±3%) and 30% (±5%) at a minimum follow-up of 7 years after distraction (n=16, p<0.0001). The same study reported mean percentages of the maximum score for AOS scores for pain of 67% (±6%) before distraction and of 25% (±6%) at a minimum follow-up of 7 years after distraction (n=16, p<0.002)[5].

In the case series of 23 patients, 61% (11/18) of patients were taking pain killers occasionally for ankle pain at mean 64-month follow-up and 78% (14/18) of patients had occasional moderate-to-mild ankle pain[6].

A case series of 26 patients treated by ankle joint distraction reported AOS pain scores (mean percentage of the maximum score ± standard deviation) of 60% (±3%) at baseline, 35% (±4%) at 1-year follow-up and 35% (±5%) at 2-year follow-up (p<0.001 for all scores versus baseline)[7].

The case series of 25 patients reported mean AOFAS pain scores of 15 (range 0 to 20) before the procedure and 31 (range 20 to 40) at a mean follow-up of 30.5 months; 91% (21/23) of patients reported a reduction in pain[8].

Limb function and mobility

In the combined analysis of the case series of 75 patients and the RCT of 36 patients, the average percentage of the maximum score for functional disability (± standard deviation) at baseline was 68% (±15%) and 36% (±23%) at 2 years after ankle distraction for the patients still included in the study (n=105); for the patients whose treatment failed (n=6), the average percentage of the maximum score for functional disability was 67% (±13%) at baseline and 71% (±18%) before treatment failure[4].

In the combined analysis of the case series of 57 patients and the RCT of 17 patients treated by joint distraction (n=9) or debridement (n=8), 1 year after the procedure, the average score for function in the case series patients increased by 69% (n=38, p<0.0001) and the average score for joint mobility increased by 8% (n=38, p value not significant). The average scores for impaired walking distance (± standard deviation) were 1.46 (±0.18) before the procedure, 0.92 (±0.20) at 1 year (n=38; p<0.03) and zero at 5 years (n=7; p<0.04). In the RCT, the average score for function increased from 19% to 61% of the maximum score (n=9; p<0.004), and the score for mobility decreased from 56% to 46% (n=9; p value not significant). At 3 years, the average score for function increased significantly by 20% compared with the average score at 1 year in the case series (n=19; p<0.03). In the 3 patients treated by distraction after debridement had failed, a 55% improvement in function was reported from the last evaluation before joint distraction[3].

The case series of 22 patients reported mean (± standard error) percentages of the maximum score for functional ability measured by clinical evaluation of 20% (±4%) before distraction and 73% (±6%) at a minimum follow-up of 7 years after distraction (n=16; p<0.001). For the AOS scores for disability the same study reported mean percentages of the maximum score before distraction of 74% (±5%), and of 32% (±7%) at a minimum follow-up of 7 years after distraction (n=16; p<0.001)[5].

The case series of 22 patients reported mean (± standard error) percentages of the range of motion of the contralateral control ankle before distraction measured by clinical evaluation of 52% (±7%) with a mean change of 34% (±23%) at a minimum follow-up of 7 years after distraction (n=16, p>0.39)[5].

In the case series of 23 patients, the mean total arc of ankle joint motion was 28º before ankle distraction and 27º after the procedure (timing not given)[6].

In the case series of 23 patients treated by ankle joint distraction, at a mean of 64 months after the procedure, 77% (14/18) of patients said that they walked for pleasure, 33% (6/18) of patients said that they could run, 22% (4/18) of patients used an assistive device to walk and 11% (2/18) of patients reported severe limitations in walking ability (no further details provided)[6].

The case series of 26 patients reported AOS disability scores (mean percentage of the maximum score ± standard deviation) of 67% (±2%) at baseline, 46% (±5%) at 1-year follow-up and 36 (±5%) at 2-year follow-up (p<0.001 for all scores compared against baseline)[7].

The case series of 25 patients reported ranges of motion before the procedure of 7º dorsiflexion (range –5º to 15º) and 32º plantarflexion (range 15º to 50º), and at a mean follow-up of 30.5 months of 4.3º dorsiflexion (range 0º to 10º) and 33º plantarflexion (range 20º to 40º); levels of significance were not stated[8].

Quality of life

In the RCT of 36 patients treated by fixed distraction or distraction with motion, the motion group had better SF-36 physical component summary scores than the fixed group at 26 weeks after fixator removal (p=0.02) and at 104 weeks after fixator removal (p=0.05), but not at 52 weeks after fixator removal (p=0.49)[1].

Patient satisfaction

In the case series of 22 patients, 1 patient reported worsened function, 13% (2/15) reported similar function, 20% (3/15) reported minimal improvement, 1 reported improvement and 53% (8/15) reported a noticeable improvement. Pain was worse in 1 patient, similar in 13% (2/16), minimally improved in 1 patient, improved in 19% (3/16) and noticeably improved in 56% (9/16). One patient was not able to answer each specific question of the Van Valburg questionnaire with respect to function[5].

In the case series of 23 patients, at a mean follow-up of 64 months, 61% (11/18) of patients were very satisfied or satisfied by the result of the procedure and 71% would recommend this procedure to a friend (absolute number not given), but 33% (6/18) were not satisfied with the outcome[6].

Treatment failure

The case series of 57 patients treated by ankle joint distraction reported that 23% (13/57) of patients withdrew from the study because of persistent pain; 62% (8/13) of these patients withdrew within 1 year after distraction. All the patients who withdrew were treated by arthrodesis[3].

The combined analysis of treatment failure in the case series of 75 patients and in the RCT of 36 patients treated by fixed ankle distraction or distraction with motion, reported treatment failure in 17% (18/105) of patients still included in the studies within 2 years after ankle distraction (6 patients were lost to follow-up). Treatment failure was defined as patients treated by arthrodesis, osteotomy or a second distraction, or patients who developed Sudeck's atrophy[4].

In the RCT of 36 patients treated by fixed distraction (n=18) or distraction with motion (n=18), conversion to arthrodesis was reported in 17% (3/18) of patients in the fixed group and in 1 patient in the motion group. In the fixed group, 1 conversion was done before the 52-week visit and 2 between the 52-week and 104-week visits; in the motion group, the conversion was done between the 52-week and 104-week visits[1].

In a 5- to10-year follow-up study of 29 patients from the RCT of 36 patients, conversion was reported in 45% (13/29) of patients: 28% (8/29) were treated by ankle arthrodesis and 17% (5/29) by total ankle arthroplasty. Of the 13 conversions, 2 were performed within 1 year after ankle distraction, 3 in the second year, 1 in the third year, 1 in the fifth year, 3 in the sixth year, 2 in the seventh year and 1 in the eighth year[2].

In the case series of 22 patients, treatment failure was reported in 27% (6/22) of patients[5].

Joint space width

The combined analysis of the case series of 57 patients and the RCT of 17 patients reported the average joint space width increased by 17% at 1 year after the procedure (n=12; p<0.04) and by 10% at 3 years compared with the mean width at 1 year (n=7; p<0.05) in the case series. This was only evaluated in patients for whom the X-ray was useful for evaluation (n=17) and who had more than 10% joint space narrowing before treatment[3].

The case series of 25 patients reported that there was no change from baseline in ankle joint space measured on X-ray at a mean follow-up of 30.5 months, in 91% (21/23) of patients[8].

Bone density

The combined analysis of the case series of 57 patients and the RCT of 17 patients treated by joint distraction or debridement reported the subchondral bone density decreased by 10% at 1 year after the procedure (n=10; p<0.03) and by an additional 7% at 3 years compared with the subchondral bone density at 1 year (n=5; p>0.23) in the case series. This was only evaluated in patients in whom the X-ray was useful for evaluation (n=17) and who had increased subchondral bone density (compared with the contralateral ankle) before treatment[3].

The case series of 26 patients reported mean changes (± standard deviation) in bone density over the area of 1 to 8 mm from the joint surface from baseline of –23% (±12%) for the tibia and –18% (±15%) for the talus at 1-year follow-up; at 2-year follow-up, the mean changes were −21% (±12%) for the tibia and −16% (±15%) for the talus (p<0.001 from baseline for all results)[7].

Safety

Thromboembolic event

Deep vein thrombosis distal to the knee was reported in 1 patient treated by ankle joint distraction in an RCT of 36 patients treated by fixed distraction (n=18) or distraction with motion (n=18); this was treated by anticoagulation therapy (no further details provided)[1].

Infection

Infection at pin sites was reported in 28% (16/57) of patients treated by ankle joint distraction in a case series of 57 patients; this was treated by antibiotics (no further details provided)[3].

Infection at pin site was reported in 33% (3/9) of patients treated by ankle joint distraction in an RCT of 17 patients treated by joint distraction (n=9) or

debridement (n=8). Pins were changed in 2 patients: 1 through the forefoot and 1 through the proximal tibia[3].

Pin track infection was reported on 43 occasions in 53% (19/36) of patients in the RCT of 36 patients treated by fixed distraction or distraction with motion. All infections were initially treated with oral antibiotics; 4 persisted and the pins were removed. Two of the 4 infections were treated by 6 weeks of intravenous antibiotics because acute osteomyelitis was suspected[1].

Infection was reported in about 75% of patients (absolute number not given) in a case series of 23 patients treated by ankle joint distraction; the patients needed at least 1 course of antibiotics during the distraction[6].

Superficial pin site infection was reported in 100% (23/23) of patients with complete data in a case series of 25 patients treated by ankle joint distraction; all infections resolved following a single course of antibiotics[8].

Numbness

Numbness in the distribution of the medial calcaneal branch of the tibial nerve and in the deep peroneal distribution onto the great toe, after the frame was fitted, was reported in 22% (8/36) of patients in the RCT of 36 patients treated by fixed distraction or distraction with motion. When numbness occurred in the context of distraction exceeding 5 mm on X-ray, the distraction was reduced to 5 mm; no other treatment was given. In 50% (4/8) of patients numbness resolved with the frame in place, 25% (2/8) resolved within 3 months after frame removal, and 25% (2/8) of patients were left with residual numbness[1].

Sudeck's atrophy

Sudeck's atrophy (reflex sympathetic dystrophy) was reported in 2% (2/105) of patients treated by ankle joint distraction who were still in the study at 2-year follow-up, in a combined analysis of a case series of 75 patients treated by ankle joint distraction and the RCT of 36 patients treated by fixed ankle distraction or distraction with motion[4].

Sudeck's atrophy was reported in 1 patient treated by ankle joint distraction in a case series of 22 patients treated by ankle joint distraction; it was unclear if this was related to the procedure[5].

Device failure

A broken pin through the forefoot, possibly caused by excessive strain during walking, was reported in 14% (8/57) of patients in the case series of 57 patients. Of these patients, 63% (5/8) had the broken pin removed and 38% (3/8) had the pin replaced; local infections were prevented or treated by antibiotics[3].

Validity and generalisability of the studies

- Limitations of the evidence base: limited number of patients and lack of RCTs.
- Maximum follow-up: 10 years[2].
- Patient overlaps between studies[1-5].

Existing assessments of this procedure

A review of the evidence on procedures available to treat ankle arthritis while preserving the joint was published by the American Orthopaedic Foot and Ankle Society in 2013[9]. It states in the conclusion: 'Distraction arthroplasty as a treatment of ankle arthritis has shown some efficacy in preliminary reports. However, the short- and long-term effectiveness of this intervention is inconclusive based on the available literature.'

A review of the literature on distraction ankle arthroplasty for the currently accepted indications was published by the American Orthopaedic Foot and Ankle Society in 2012[10]. It states in the conclusion: 'A comprehensive review of the literature has provided predominantly Level V evidence with far fewer Level II, III and IV trials for the generally accepted indications for distraction ankle arthroplasty. There was no level I evidence. The evidence available has created a grade I recommendation for the use of the procedure in all of its generally accepted indications. More high quality, scientific studies are needed to discover the true value of distraction ankle arthroplasty.'

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.

NICE guidelines

- Osteoarthritis: care and management in adults. NICE guideline CG177 (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. Six

Specialist Advisor Questionnaires for joint distraction for ankle osteoarthritis were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 10 questionnaires to 1 NHS trust for distribution to patients who had the procedure (or their carers). NICE received 2 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Issues for consideration by IPAC

- No ongoing trials.
- IP 1273 (Joint distraction for knee osteoarthritis without alignment correction) is in development.

References

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Appendix A: Additional papers on joint distraction for ankle osteoarthritis

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
D'Angelantonio AM and Schick FA. (2013) Ankle distraction arthroplasty combined with joint resurfacing for management of an osteochondral defect of the talus and concomitant osteoarthritis: a case report. Journal of Foot & Ankle Surgery 52:76-79.	Single case report FU=6 months	The patient reported a decrease in ankle joint pain, increased range of motion, and a return to normal daily activity without limitation.	Studies with more patients or longer follow-up are included.
Inda DJ, Blyakher A, O'Malley MJ et al. (2003) Distraction arthroplasty for the ankle using the Ilizarov frame. Techniques in Foot and Ankle Surgery 2(4):249-253.	Case series n=9 FU=mean 1 year	All patients had improvement in the radiographic appearance of the ankle. A wider joint space was reported in all patients. Patients were all satisfied with the procedure and all reported improvement in pain. Ankle dorsi-flexion improved as well. Overall arc of motion did not substantially improve. Most common complication: superficial pin site infection.	Studies with more patients or longer follow-up are included.
Nakasa T, Adachi N, Kato T et al. (2015) Distraction arthroplasty with arthroscopic microfracture in a patient with rheumatoid arthritis of the ankle joint. Journal of Foot & Ankle Surgery 54:280-284.	Single case report FU=2 years	After 3 months, removal of the external device and repeat arthroscopy revealed newly formed fibrocartilage on the surfaces of both the tibia and the talus. At 2 years after the surgery, a radiograph showed that the joint space enlargement of the ankle had been maintained. The American Orthopaedic Foot and Ankle Society score improved from 37 points preoperatively to 82 points at 2 years postoperatively.	Studies with more patients or longer follow-up are included.
Ugaji S, Watanabe K, Matsubara H et al. (2014) Simultaneous arthrodiastasis and deformity correction for a patient with ankle osteoarthritis and lower limb deformity: a case report. Journal of Foot & Ankle Surgery 20:74-78.	Single case report FU=2 years	The patient had an improved clinical score of 98 points at a 2-year follow-up	Studies with more patients or longer follow-up are included.
van Valburg AA, van Roermund PM, Lammens J et al. (1995) Can Ilizarov joint distraction delay the need for an arthrodesis of the ankle? A preliminary report. Journal of Bone & Joint	Case series n=11 FU=mean 2 years	Distraction for 3 months resulted in clinical improvement in pain and mobility for a mean of 2 years, with an increase in the joint space	Studies with more patients or longer follow-up are included.

Surgery - British Volume 77:720-725.			
Van Valburg AA, van Roermund PM, Marijnissen AC et al. (1999) Joint distraction in treatment of osteoarthritis: a two-year follow-up of the ankle. Osteoarthritis & Cartilage 7:474-479.	Case series n=17 FU=2 years	More than 2 thirds of the patients improved significantly as shown by physical examination, functional ability questionnaires and pain scale; effects were progressive in the second year of follow-up. On average, joint mobility and radiographic joint space were preserved, whilst improvement was observed in a significant number of patients.	Studies with more patients or longer follow-up are included. Patients most likely already included in Ploegmakers 2005 study (in table 2). No numerical data.

Appendix B: Related NICE guidance for joint distraction for ankle osteoarthritis

Guidance	Recommendations
NICE guidelines	**Osteoarthritis: care and management. NICE guideline CG177 (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 ankle osteoarthritis

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	27/08/2015	Issue 8 of 12, August 2015
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	27/08/2015	Issue 7 of 12, July 2015
HTA database (Cochrane Library)	27/08/2015	Issue 3 of 4, July 2015
MEDLINE (Ovid)	27/08/2015	1946 to August week 3 2015
MEDLINE In-Process (Ovid)	27/08/2015	August 26, 2015
EMBASE (Ovid)	27/08/2015	1974 to 2015 week 34
PubMed	27/08/2015	n/a
JournalTOCS	28/08/2015	n/a

Trial sources searched on

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials metaRegister of Controlled Trials – mRCT
- Clinicaltrials.gov

Websites searched on

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference websites <<add details>>
- 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/
2 ankle/
3 1 and 2
4 ((ankle* or tarocrural*) adj4 (osteoarthrit* or cartilag* or degenerat* or detoriat* or OA)).ti,ab.
5 ((degenerativ* or arthritis*) adj4 ankle*).ti,ab.
6 or/3-5
7 arthrodiatas*.ti,ab.
8 ((realign* or re-align*) adj4 osteotom*).ti,ab.
9 ((joint* or bone*) adj4 (arthroplast* or distract* or separat* or pull* or move* or apart* or align* or realign* or re-align*)).ti,ab.
10 Arthroplasty, Replacement, Ankle/
11 AJD.ti,ab.
12 ilizarov technique/ or osteogenesis, distraction/
13 ((osteogenesis* or call* or callotas* or osteodistract*) adj4 Distract*).ti,ab.
14 (ilizarov* adj4 (techni* or method* or apparat* or fix* or frame*)).ti,ab.
15 (RingFIX or ((Rozbruch adj4 Ankle* adj4 Distract*) or RAD)).ti,ab.
16 or/7-15
17 6 and 16
18 Animals/ not Humans/
19 17 not 18