NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of magnetic resonance therapy for knee osteoarthritis

Osteoarthritis can develop in the knee when cartilage covering the ends of the bone becomes worn. This can cause pain, stiffness, swelling and difficulty walking. In this procedure, a magnetic resonance device is put over the knee. The device produces electromagnetic energy, stimulating the cartilage to heal . Treatments last about an hour and are given for 5 to 10 days in a row. The aim is to relieve the symptoms of osteoarthritis.

Contents

Abbreviations

Word or phrase	Abbreviation
Confidence interval	CI
Femoral condylar cartilage thickness	FCT
Femoral intercondylar area	FICA
Lateral femoral condyle	LFC
Magnetic resonance therapy	MRT
Medial femoral condyle	MFC
Mental component score	MCS
Molecular biophysical stimulation therapy	MBST
Not statistically significant	NS
Nuclear magnetic resonance	NMR
Osteoarthritis	OA
Physical component score	PCS
Short form 36	SF-36
Standard deviation	SD
Visual analogue scale	VAS
Western Ontario and McMaster Universities Artritis Index	WOMAC

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure 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 professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in August 2020.

Procedure name

- magnetic resonance therapy for knee osteoarthritis

Professional societies

- British Orthopaedic Association
- British Association for Surgery of the Knee (BASK)
- British Society of Rheumatology
- Chartered Society of Physiotherapists (CSP).

Description of the procedure

Indications and current treatment

Osteoarthritis of the knee is the result of progressive deterioration of the articular cartilage and menisci of the joint, usually because of trauma and wear and tear. This leads to exposure of the bone surface. Symptoms include pain, stiffness, swelling and difficulty walking. Acute exacerbations of pain are common and usually self-limiting after 14 days. Only a small number of patients develop progressive symptoms needing treatment.

Treatment depends on the severity of the symptoms. 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 and unicompartmental or total knee replacement.

What the procedure involves

Magnetic resonance therapy for osteoarthritis (MRT) is a non-invasive procedure that uses a special device to administer electromagnetic energy to an osteoarthritic joint. A range of devices with different physical designs are available. The aim is to relieve the symptoms and to improve the osteoarthritis by stimulating the cartilage cells.

MRT is done in an outpatient setting. During the procedure, the patient lies on the couch and a section of the MRT device slides over the knee. The device generates electromagnetic fields which are targeted to the cartilaginous tissue in the affected joint. The aim is to promote joint repair and relieve the symptoms of osteoarthritis. Each treatment lasts 60 minutes. Depending on the severity of the

disease and MRT therapy device, a course of treatment typically consists of 5 to 10 treatment sessions on consecutive days.

Outcome measures

Lequesne index

The Lequesne index is a questionnaire used to evaluate the severity of the osteoarthritis. It has 5 questions relating to pain or discomfort, 1 question about the maximum distance walked, and 4 questions about activities of daily living. The total questionnaire is scored on a 0 to 24 scale. Lower scores indicate there is less functional impairment.

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 to 20); stiffness (score range 0 to 8) and physical function (score range 0 to 68). The total score ranges from 0 to 96 with lower scores indicating better outcomes.

Efficacy summary

Osteoarthritis symptoms

Lequesne osteoarthritis (OA) index

In a survey of 2,770 patients with knee OA, there was a statistically significant decrease in the mean global score for the Lequesne OA index from 7.77 ± 4.33 before the procedure to 6.62 ± 3.92 after the procedure, 5.70 ± 3.87 at 3 months, 4.97 ± 3.86 at 6 months and 4.69 ± 3.94 at 12 months ($p<0.000001$). The statistically significant improvement was reported for each of the 3 components of the index (pain/complaints, walking distance and function, $p<0.000001$).[1]

WOMAC index

WOMAC-pain score

In a randomised controlled trial (RCT) of 97 patients with mild to moderate knee OA (49 patients who had MRT compared with 48 patients who had placebo therapy), there were statistically significant improvements from baseline in mean WOMAC-pain scores for both MRT and placebo at 2 and 12 weeks. For MRT, mean WOMAC-pain scores decreased from 4.25 ± 2.08 to 2.16 ± 2.09 at 2

weeks and to 2.26 ± 2.11 at 12 weeks (p<0.001). For placebo therapy, mean WOMAC-pain scores decreased from 4.08 ± 2.09 to 2.16 ± 2.36 at 2 weeks and to 2.50 ± 2.09 at 12 weeks (p<0.001). However, there were no statistically significant differences between MRT and placebo for the improvements in WOMAC-pain scores at 2 weeks (-2.09 ± 2.15 compared with -1.91 ± 2.49, p=0.712) and at 12 weeks (-1.98 ± 2.13 compared with -1.58 ± 2.13, p=0.351). [2]

WOMAC-stiffness score

In the RCT of 97 patients, there were statistically significant improvements from baseline in mean WOMAC-stiffness scores for both MRT and placebo at 2 and 12 weeks. For MRT, mean WOMAC-stiffness scores decreased from 3.46 ± 2.16 to 1.65 ± 1.84 at 2 weeks and to 1.54 ± 1.60 at 12 weeks (p<0.001). For placebo therapy, mean WOMAC-stiffness scores decreased from 2.96 ± 2.38 to 1.69 ± 2.02 at 2 weeks and to 1.84 ± 1.94 at 12 weeks (p<0.001). However, there were no statistically significant differences between MRT and placebo for the improvements in WOMAC-stiffness scores at 2 weeks (-1.81 ± 2.12 compared with -1.27 ± 2.12, p=0.213) and at 12 weeks (-1.92 ± 2.20 compared with -1.1 ± 2.03, p=0.660). [2]

WOMAC-physical function score

In the RCT of 97 patients, there were statistically significant improvements from baseline in mean WOMAC-physical function scores for both MRT and placebo at 2 and 12 weeks. For MRT, mean WOMAC-physical function scores decreased from 4.27 ± 2.02 to 2.31 ± 1.90 at 2 weeks and to 2.48 ± 2.09 at 12 weeks (p<0.001). For placebo therapy, mean WOMAC-physical function scores decreased from 3.88 ± 2.36 to 2.34 ± 2.28 at 2 weeks and to 2.25 ± 1.77 at 12 weeks (p<0.001). However, there were no statistically significant differences between MRT and placebo for the improvements in WOMAC-physical function scores at 2 weeks (-1.96 ± 1.87 compared with -1.54 ± 2.56, p=0.361) and at 12 weeks (-1.79 ± 1.81 compared with -1.63 ± 2.32, p=0.700). [2]

Pain

In the survey of 2,770 patients with knee OA, peak pain, pain on load and pain at rest scores measured on a visual analogue scale decreased statistically significantly after the 9 nuclear magnetic resonance (NMR) treatment sessions, with further reductions after 3, 6, and 12 months (p<0.00001). The pain frequency also decreased with all 3 types of pain, especially 6 and 12 months after NMR therapy. Pain on load diminished on a 10-part scale from 6 (daily) to 4 (once a week), the frequency of peak pain reduced to ‘very little/only twice a month’ (= 3), and pain at rest decreased to ‘rare’ to ‘very rare’ (as stated in the article). The number of patients who had no complaints during the night increased from 39% at baseline to 72% 12 months after NMR therapy. The

percentage of patients without pain when walking increased from 24% to 48%. One year after treatment, 32% of patients could kneel or crouch down without any difficulty, while at baseline this was possible for only 15% of patients [1]

In the RCT of 97 patients, there were statistically significant improvements from baseline in mean VAS pain scores (from 0 [no pain] to 10 [worst pain]) for both MRT and placebo at 2 and 12 weeks. For MRT, mean VAS-pain scores decreased from 6.36 ± 2.24 to 3.76 ± 3.16 at 2 weeks and to 3.75 ± 3.14 at 12 weeks ($p<0.001$). For placebo therapy, mean VAS-pain scores decreased from 4.91 ± 6.06 to 2.90 ± 4.80 at 2 weeks and to 2.86 ± 4.40 at 12 weeks ($p<0.001$). However, there were no statistically significant differences between MRT and placebo for the improvements in VAS-pain scores at 2 weeks (-2.6 ± 3.35 compared with -1.63 ± 3.35, $p=0.160$) and at 12 weeks (-2.61 ± 3.19 compared with -1.85 ± 3.42, $p=0.263$). In the same study, there was no significant difference in paracetamol consumption between MRT and placebo during the study. [2]

Range of motion

In the survey of 2,770 patients with knee OA, statistically significant improvements in the active range of motion were recorded 3 months after NMR therapy ($p<0.000001$), with a further enhancement of flexion and extension after 6 and 12 months. [1]

Quality of life

SF-36 physical component score

In the RCT of 97 patients, there were statistically significant improvements from baseline in mean SF-36 physical component scores (from 0 [worst quality of life to 100 [best quality of life]) for both MRT and placebo at 2 and 12 weeks. For MRT, mean SF-36 physical component scores increased from 29.79 ± 8.53 to 39.14 ± 10.82 at 2 weeks and to 39.06 ± 12.47 at 12 weeks ($p<0.001$). For placebo therapy, mean SF-36 physical component scores increased from 33.09 ± 9.40 to 35.85 ± 43.10 at 2 weeks and to 37.89 ± 44.91 at 12 weeks ($p<0.001$). However, there were no statistically significant differences between MRT and placebo for the improvements in SF-36 physical component scores at 2 weeks (9.35 ± 8.70 compared with 6.37 ± 11.59, $p=0.158$) and at 12 weeks (9.2 ± 9.94 compared with 8.3 ± 12.30, $p=0.673$). [2]

SF-36 mental component score

In the RCT of 97 patients, there was a statistically significant improvement from baseline in mean SF-36 mental component scores (from 0 [worst quality of life to 100 [best quality of life]) for MRT at 12 weeks only from 49.80 ± 12.38 to 54.50 ±

10.16 (p=0.006). For placebo therapy, the increase in mean SF-36 mental component scores was statistically significant at 2 weeks but not at 12 weeks: 45.87 ± 12.50 compared with 52.20 ± 11.98 (p=0.002 at 2 weeks). There were no statistically significant differences between MRT and placebo for the improvements in SF-36 mental component scores at 2 weeks (2.64 ± 12.55 compared with 6.32 ± 13.09, p=0.161) and at 12 weeks (4.69 ± 11.3 compared with 2.1 ± 10.93, p=0.255). [2]

Cartilage thickness

In the RCT of 97 patients, there were no statistically significant differences in femoral condylar cartilage thickness measured with ultrasound in the treated and in the untreated knees between MRT and placebo at baseline and 12 weeks after treatment. In the same study, there were no statistically significant differences in whole-organ MRI scores after surgery compared with baseline for MRT and placebo. [2]

In a case series of 14 patients, there were statistically significant improvements after the procedure in the mean cartilage thickness of the patella (1.93 mm ± 0.37 mm compared with 2.24 mm ± 0.39 mm, p<0.001), in the maximum cartilage thickness of the patella (4.14 mm ± 0.81 mm compared with 4.52 mm ± 0.88 mm, p<0.05), in the minimum cartilage thickness of the patella (0.02 mm ± 0.08 mm compared with 0.11 mm ± 0.16 mm, p<0.05), and in the volume of the cartilage of the patella (2,109.28 mm^3 ± 660.75 mm^3 compared with 2,459.48 mm^3 ± 655.60 mm^3, p<0.001). However, there was no significant change in the surface of the cartilage of the patella (912.67 mm^2 ± 170.34 mm^2 compared with 942.45 mm^2 ± 179.73 mm^2, not significant). For the tibia, there were statistically significant improvements after the procedure in the mean thickness of the medial cartilage (1.25 mm ± 0.30 mm compared with 1.37 mm ± 0.26 mm, p<0.05) and of the lateral cartilage (1.64 mm ± 0.49 mm compared with 1.67 mm ± 0.35 mm, p<0.01); in the maximum thickness of the medial cartilage (2.42 mm ± 0.60 mm compared with 2.63 mm ± 0.43 mm, p<0.05) and of the lateral cartilage (3.30 mm ± 0.98 mm compared with 3.38 mm ± 0.73 mm, p<0.01), and in the volume of the medial cartilage (1,343.36 mm^3 ± 446.61 mm^3 compared with 1,511.67 mm^3 ± 342.49 mm^3, p<0.05) and of the lateral cartilage (1,706.83 mm^3 ± 630.84 mm^3 compared with 1,739.23 mm^3 ± 453.24 mm^3, p<0.05). There were no significant changes after the procedure in the minimum medial cartilage thickness, and in the medial and lateral cartilage surfaces. The results were not clear for the minimal thickness of the lateral cartilage structure of the tibia. For the femur, none of the changes measured for the cartilage thickness were significant. [3]

Safety summary

No adverse effects were reported during follow up in the RCT of 97 patients. [2]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, we received no questionnaires.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to magnetic resonance therapy for knee osteoarthritis. The following databases were searched, covering the period from their start to 18 August 2020: 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 the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria shown in the following table 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.

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	Magnetic resonance therapy.
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 2,881 patients from 1 survey, 1 RCT and 1 case series.[1-3]

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on magnetic resonance therapy for knee osteoarthritis

Study 1 Kullich W (2013)

Study details

Study type	Survey
Country	Germany and Austria (61 centres)
Recruitment period	2000 to 2010
Study population and number	n=4,518 patients including **2,770 patients with osteoarthritis of the knee**, 673 patients with osteoarthritis of the hip, 420 patients with osteoarthritis of the ankle joint and 655 patients with low back pain.
Age and sex	OA of the knee: mean 62 years; 58% (1,609/2,770) female OA of the hip: mean 65 years; 51% (343/673) female OA of the ankle joint: mean 59 years; not reported Low back pain: mean 63 years; 62% (408/655) female
Patient selection criteria	The diagnoses of OA of the knee, OA of the hip, OA of the ankle, and low back pain were verified by radiological diagnostics. Included patients had given their informed consent for data collection and had been treated with nuclear magnetic resonance in accordance with the indications mentioned above.
Technique	Therapeutic nuclear magnetic resonance with devices belonging to the company Wetzlar, Germany. The nuclear field consists of 3 matched fields: (a) main magnetic field, (b) variable, modulating sweep-field, (c) alternating magnetic field at the Larmor frequency vertically to (a) and (b). It is generated in a Helmholtz coil with a permanent basic field up to 40 mT and a dynamic field strength of radiofrequency up to 2.3 mT. The nuclear magnetic resonance frequency is about 17 to 85 kHz. The applicators of the therapy systems respond to a central control unit according to a chipcard which is programmed for the special parameters adapted for tissue and indication. The duration of the treatment totalled up to 9 therapy units for 1 hour each on consecutive days.
Follow-up	1 year
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Patients were followed up immediately after treatment, 6 to 8 weeks, 6 months, and 1 year after treatment.

Study design issues: Evaluation criteria were pain at rest, pain on load, and peak pain, measured with a visual analogue scale (VAS). Further evaluation of clinical success was done using validated function indices covering disability, function deficit and restrictions of everyday functions. The collected data were entered centrally (IEB – Institute for Development of New Therapy Methods, Wetzlar, Germany).

Study population issues: For the knee OA indication, there were 46 % of patients who were overweight and 22% who were obese. the mean BMI of obese patients was 33.9 ± 4.0.

Other issues: The numbers from the figures representing the improvements in knee flexion and in pain symptoms were not reported.

Key efficacy findings

Number of patients analysed: 2,770

Lequesne OA index (mean ± SD [median])

Lequesne OA index	Before NMR	After NMR	3 months	6 months	12 months
Global score	7.77 ± 4.33 (7.50)	6.62 ± 3.92 (6.50)	5.70 ± 3.87 (5.50)	4.97 ± 3.86 (4.50)	4.69 ± 3.94 (4.00)
Pain/complaints (1st component)	3.05 ± 1.86 (3.00)	2.52 ± 1.75 (2.00)	2.03 ± 1.62 (2.00)	1.74 ± 1.63 (1.00)	1.58 ± 1.64 (1.00)
Walking distance (2nd component)	1.80 ± 1.66 (1.00)	1.63 ± 1.50 (1.00)	1.49 ± 1.47 (1.00)	1.29 ± 1.34 (1.00)	1.21 ± 1.24 (1.00)
Function (3rd component)	2.92 ± 1.82 (3.00)	2.47 ± 1.64 (2.00)	2.18 ± 1.63 (2.00)	1.94 ± 1.63 (2.00)	1.89 ± 1.74 (2.00)

There was a statistically significant improvement in Lequesne index after the procedure and during follow up ($p<0.000001$).

The global score ranges from 0 (no pain, no disability) to 24 (maximum pain, stiffness, and disability). For each of the 3 sections, the score ranges from 0 to 8.

Pain

- Peak pain, pain on load and pain at rest scores measured on a visual analogue scale decreased statistically significantly after the 9 NMR treatment sessions, with further reductions after 3, 6, and 12 months ($p<0.00001$).

- The pain frequency also decreased with all 3 types of pain, especially 6 and 12 months after NMR therapy. Pain on load diminished on a 10-part scale from 6 (daily) to 4 (once a week), the frequency of peak pain

reduced to “very little/only twice a month” (= 3), and pain at rest decreased to “rare” to “very rare” (as written in the article).

- The number of patients with osteoarthritis of the knee who had no complaints during the night increased from 39% at baseline to 72% 12 months after NMR therapy.
- Regarding walking, the pain-free group increased from 23.5% to 48.2%.
- One year after treatment, 31.9% of patients with osteoarthritis of the knee could kneel or crouch down without any difficulty, at baseline this was possible for only 14.9% of patients.

Range of motion

- Three months after NMR therapy, statistically significant improvements in the active range of motion were recorded ($p<0.000001$), with a further enhancement of flexion and extension after 6 and 12 months.

Key safety findings

Not reported.

Study 2 Goksen N (2016)

Study details

Study type	Randomised double-blind placebo-controlled trial
Country	Turkey (single centre)
Recruitment period	2012 to 2013
Study population and number	n=97 (49 MRT versus 48 placebo) Patients with mild to moderate knee OA.
Age and sex	Mean 54 years; 81% (79/97) female
Patient selection criteria	Inclusion criteria: consecutive patients who met the American College of Rheumatology classification criteria for knee OA, age between 35 [30 written in the abstract] and 75 years, symptomatic OA of a single knee, radiological stage of 2 or 3 according to Kellgren and Lawrence scale. Exclusion criteria: cardiac arrhythmias or failure and symptomatic pulmonary diseases, uncontrolled hypertension, history of knee surgery or any inflammatory rheumatic disease, malignancy or trauma of the knee joints, pregnancy, active infection of the knee or adjacent soft tissues, treatment with viscosupplementation within the last year, or contraindications for magnetic resonance and magnetic fields like use of cardiac pacemakers.
Technique	Patients using NSAIDs or supplementary therapies were asked to stop their medication at least 2 weeks before having MRT and were only allowed to take paracetamol tablets. Device used: NuclearMagneticReseonance Therapy, MBST® Open System 350, Medtec Medizitechnik GmbH, Wetzlar, Germany. The nuclear MR frequency was about 17 to 85 kHz. During the placebo treatment, only the led were active but there were no pulses. The patients were treated for 1 hour daily on all weekdays for 2 weeks. Patients were checked for compliance every week for 2 weeks of treatment.
Follow-up	12 weeks
Conflict of interest/source of funding	This study was supported with a grant from the Research Fund of the Erciyes University. The authors certified that there is no conflict of interest.

Analysis

Follow-up issues:

- All patients had clinical examinations at baseline, 2 weeks and 12 weeks after the procedure. Imaging included blindly assessed ultrasonography and MR of the knee.

- From 152 patients assessed for eligibility, 100 had been randomised to MRT or placebo. In the MRT group, 1 patient did not have the procedure because of a lack of time. In the placebo group, 2 patients did not have the placebo procedure because of a lack of time and a change in address.

- MR scans of 44 patients who had MRT and of 43 patients who had the placebo were taken at baseline and follow up.

- Two patients who had MRT and 3 patients who had the placebo were 1 day off the treatment.

Study design issues:

- The physiotherapist applying MRT or placebo, the assessors and the radiologist scoring the MR scans were all blinded to the group assignment. For randomisation, the manufacturer of the MRT device provided coded individual chips to operate the machine and a sealed envelope with serial numbers and randomly assigned corresponding groups. Fifty chips were signal negative and 50 chips were signal positive.

- The main outcome measures were: pain (assessed with a visual analogue scale), quality of life (assessed with the SF-36) and physical functions (assessed with the WOMAC Likert scale).

- The X-rays were scored using the Kellgren-Lawrence scoring system. The cartilage thickness was measured using ultrasonography. Whole organ MRI score (WORMS) was used to evaluate cartilage signal and morphology. Marrow abnormalities, bone cysts, bone attrition, osteophytes, lesion of menisci, ligaments and synovitis were also evaluated.

Key efficacy findings

- Number of patients analysed: 97 (49 MRT versus 48 placebo)

Pain - VAS (from 0 to 10, lower scores indicate better outcomes)

Changes in VAS-pain from baseline to after the procedure	MRT			Placebo		
	Mean (SD)	**95% CI**	**p value**	**Mean (SD)**	**95% CI**	**p value**
Baseline	6.36 (2.24)	5.72 to 7.01		5.48 (1.99)	4.91 to 6.06	
2 weeks	3.76 (3.16)	2.85 to 4.67	**<0.001**	3.85 (3.20)	2.90 to 4.80	**<0.001**
12 weeks	3.75 (3.14)	2.85 to 4.65	**<0.001**	3.63 (2.65)	2.86 to 4.40	**<0.001**

Reductions in VAS-pain scores from baseline to 2-week or 12-week follow up were statistically significant for both MRT and placebo.

Differences in VAS-pain compared between groups	MRT		Placebo		p value
	Mean (SD)	95% CI	Mean (SD)	95% CI	
Difference between baseline and week 2* *corrected by analyst	-2.6 (3.35)	-3.56 to -1.63	-1.63 (3.35)	-2.61 to -0.66	0.160
Difference between baseline and week 12	-2.61 (3.19)	-3.53 to -1.69	-1.85 (3.42)	-2.84 to -0.86	0.263

There were no statistically significant differences between groups for the improvements in VAS-pain scores at 2 and 12 weeks.

Physical function - WOMAC (higher scores indicate worse outcomes)

Changes in WOMAC from baseline to after the procedure	MRT			Placebo		
	Mean (SD)	95% CI	p value	Mean (SD)	95% CI	p value
WOMAC-pain						
Baseline	4.25 (2.08)	3.65 to 4.85		4.08 (2.09)	3.47 to 3.69	
2 weeks	2.16 (2.09)	1.56 to 2.76	**<0.001**	2.16 (2.36)	1.47 to 2.85	**<0.001**
12 weeks	2.26 (2.11)	1.65 to 2.87	**<0.001**	2.50 (2.09)	1.89 to 3.10	**<0.001**
WOMAC-stiffness						
Baseline	3.46 (2.16)	2.84 to 4.09		2.96 (2.38)	2.27 to 3.66	
2 weeks	1.65 (1.84)	1.12 to 2.18	**<0.001**	1.69 (2.02)	1.11 to 2.28	**<0.001**
12 weeks	1.54 (1.60)	1.08 to 2.00	**<0.001**	1.84 (1.94)	1.28 to 2.41	**<0.001**
WOMAC-physical function						
Baseline	4.27 (2.02)	3.69 to 4.85		3.88 (2.36)	3.19 to 4.57	
2 weeks	2.31 (1.90)	1.76 to 2.86	**<0.001**	2.34 (2.28)	1.68 to 3.00	**<0.001**
12 weeks	2.48 (2.09)	1.87 to 3.08	**<0.001**	2.25 (1.77)	1.73 to 2.77	**<0.001**

Reductions in WOMAC scores from baseline to 2-week or 12-week follow up were statistically significant for both MRT and placebo.

Differences in WOMAC compared between groups	MRT		Placebo		p value
	Mean (SD)	95% CI	Mean (SD)	95% CI	
WOMAC-pain					
Difference between baseline and week 2* *corrected by analyst	-2.09 (2.15)	-2.71 to -1.47	-1.91 (2.49)	-2.64 to -1.19	0.712
Difference between baseline and week 12	-1.98 (2.13)	-2.60 to -1.37	-1.58 (2.13)	-2.20 to -0.96	0.351
WOMAC-stiffness					
Difference between baseline and week 2* *corrected by analyst	-1.81 (2.12)	-2.42 to -1.20	-1.27 (2.12)	-1.88 to -0.65	0.213
Difference between baseline and week 12	-1.92 (2.20)	-2.55 to -1.28	-1.1 (2.03)	-1.71 to -0.52	0.660
WOMAC-physical function					
Difference between baseline and week 2* *corrected by analyst	-1.96 (1.87)	-2.49 to -1.42	-1.54 (2.56)	-2.28 to -0.79	0.361
Difference between baseline and week 12	-1.79 (1.81)	-2.31 to -1.27	-1.63 (2.32)	-2.30 to -0.95	0.700

There were no statistically significant differences between groups for the improvements in WOMAC index scores at 2 and 12 weeks.

Quality of life – SF-36 (higher scores indicate more favourable health states)

Changes in SF-36 score from baseline to after the procedure	MRT			Placebo		
	Mean (SD)	95% CI	p value	Mean (SD)	95% CI	p value
SF-36 (PCS)						
Baseline	29.79 (8.53)	27.34 to 32.24		33.09 (9.40)	30.35 to 35.85	
2 weeks	39.14 (10.82)	36.03 to 42.25	**<0.001**	39.47 (12.40)	35.85 to 43.10	**<0.001**
12 weeks	39.06 (12.47)	35.47 to 42.64	**<0.001**	41.40 (12.90)	37.89 to 44.91	**<0.001**
SF-36 (MCS)						
Baseline	49.80 (12.38)	46.24 to 53.36		45.87 (12.50)	42.23 to 49.51	
2 weeks	52.45 (11.91)	49.03 to 55.87	0.146	52.20 (11.98)	48.72 to 55.68	**0.002**
12 weeks	54.50 (10.16)	51.57 to 57.42	**0.006**	47.98 (13.12)	44.17 to 51.79	0.18

Differences in SF-26 scores compared between groups	MRT		Placebo		p value
	Mean (SD)	95% CI	Mean (SD)	95% CI	
SF-36 (PCS)					
Difference between baseline and week 2 [corrected by analyst]	9.35 (8.70)	6.85 to 11.85	6.37 (11.59)	3.01 to 9.74	0.158
Difference between baseline and week 12	9.2 (9.94)	6.41 to 12.12	8.3 (12.30)	4.72 to 11.88	0.673
SF-36 (MCS)					
Difference between baseline and week 2 [corrected by analyst]	2.64 (12.55)	-0.95 to 6.25	6.32 (13.09)	2.52 to 10.12	0.161
Difference between baseline and week 12	4.69 (11.3)	1.44 to 7.94	2.1 (10.93)	-1.06 to 5.28	0.255

There was no statistically significant difference between groups.

Femoral condylar cartilage thickness (ultrasonographic measurement, unit not specified)

Changes in FCT from baseline to 12 weeks after the procedure	MRT		Placebo		p value
	Mean (SD)	95% CI	Mean (SD)	95% CI	
Treated knee					
LFC at baseline	1.90 (0.29)	1.82 to 1.99	1.92 (0.33)	1.81 to 2.00	0.840
LFC at 12 weeks	1.92 (0.26)	1.84 to 1.99	1.92 (0.34)	1.82 to 2.03	0.918
FICA at baseline	2.07 (0.38)	2.07 to 1.96	2.19 (0.42)	2.06 to 2.30	0.158
FICA at 12 weeks	2.01 (0.32)	1.92 to 2.11	2.09 (0.41)	1.97 to 2.21	0.299
MFC at baseline	1.95 (0.35)	1.84 to 2.05	1.94 (0.37)	1.83 to 2.05	0.969
MFC at 12 weeks	1.92 (0.30)	1.83 to 2.00	1.88 (0.36)	1.77 to 1.99	0.568
Untreated knee					
LFC at baseline	1.87 (0.3)	1.78 to 1.95	1.90 (0.3)	1.80 to 1.98	0.628

LFC at 12 weeks	1.90 (0.25)	1.83 to 1.98	1.88 (0.30)	1.78 to 1.96	0.644
FICA at baseline	2.08 (0.36)	1.97 to 2.18	2.20 (0.35)	2.09 to 2.31	0.930
FICA at 12 weeks	2.05 (0.36)	1.95 to 2.16	2.07 (0.33)	1.97 to 2.17	0.851
MFC at baseline	1.89 (0.3)	1.80 to 1.97	1.96 (0.35)	1.84 to 2.05	0.301
MFC at 12 weeks	1.94 (0.28)	1.86 to 2.02	1.88 (0.34)	1.78 to 1.98	0.362

There were no statistically significant differences in femoral condylar cartilage thickness between MRT and placebo at baseline and 12 weeks after treatment.

Whole-organ MRI score (WORMS, higher scores indicate worse outcomes)

	Before surgery		**12 weeks after surgery**		**Δ**	**P value**
	Mean (SD)	95% CI	Mean (SD)	95% CI		
MRT (n=44)	33.60±32.38	23.75 to 43.44	33.89±32.94	23.87 to 43.90	-0.28	0.577
Placebo (n=43)	20.91±21.73	14.22 to 27.59	21.19±22.40	14.29 to 28.08	-0.28	0.634

There were no statistically significant differences in WORMS scores after surgery compared with baseline for MRT and placebo.

Analgesic consumption during the study

	MRT (% of patients)	**Placebo (% of patients)**
No paracetamol consumption	57.1%	60.4%
1 to 5 paracetamol tablets	18.4%	20.8%
4 to 10 paracetamol tablets	14.3 %	6.2%
10 to 15 paracetamol tablets	4.1%	0%
More than 15 paracetamol tablets	6.1%	12.5%

There was no significant difference in the paracetamol consumption between MRT and placebo groups.

Key safety findings

The journal article states that ‘no adverse effects on patients were reported during the follow-up period’.

Study 3 Froböse I (2000)

Study details

Study type	Case series
Country	Germany
Recruitment period	Not reported
Study population and number	n=14 Patients with knee OA (stages 2 and 3)
Age and sex	Mean 54 years; 100% (14/14) female
Patient selection criteria	Patients with stages 2 and 3 knee OA who reported discomfort in the knee joint for more than 10 years and who had symptoms such as pain and mobility reduction. Exclusion criteria: pregnancy, presence of any electronic implant, presence of metal in the area of treatment, and heart disorder.
Technique	MultiBioSignal Therapy with the MBST 1-CELLREMAKE device from the company MedTec Medizintechnik. The therapy consisted of 9 treatments sessions of 1 hour each. They were carried out on consecutive days with a break at the weekend. For the treatment, the knee joint was rested in a specially designed treatment coil which was controlled by a control unit. Through the control unit, the treatment coil received the commands to generate the complex therapy fields that are typical for the MBS therapy. The control unit did also guarantee a predefined standard of therapy.
Follow-up	'After therapy'
Conflict of interest/source of funding	Not reported

Analysis

Study design issues:

- The main outcomes were the volume of the cartilage and its thickness before and after the therapy. The cartilage thickness was calculated using a 3D algorithm. The statistical evaluation was carried out with a T-Test for dependent random samples, using SPSS.

- The authors wrote that there were problems related to the measurement technology for the femur cartilage thickness evaluation that could partially explain that the changes in cartilage thickness for the femur did not show statistical significance.

Key efficacy findings

- Number of patients analysed: 14

Cartilage thickness of the patella (mean ± SD)

Clinical outcome	Before therapy	After therapy	p value
Mean thickness (mm)	1.93 ± 0.37	2.24 ± 0.39	**<0.001**
Maximum thickness (mm)	4.14 ± 0.81	4.52 ± 0.88	**<0.05**
Minimum thickness (mm)	0.02 ± 0.08	0.11 ± 0.16	**<0.05**
Volume (mm^3) interpolated	2109.28 ± 660.75	2459.48 ± 655.60	**<0.001**
Area (mm^2) Cartilage-Bone boundary	912.67 ± 170.34	942.45 ± 179.73	NS

Cartilage thickness of the tibia (mean ± SD)

Clinical outcome	Before therapy	After therapy	p value
Medial cartilage structure of the tibia			
Mean thickness (mm)	1.25 ± 0.30	1.37 ± 0.26	**<0.05**
Maximum thickness (mm)	2.42 ± 0.60	2.63 ± 0.43	**<0.05**
Minimum thickness (mm)	0.29 ± 0.08	0.31 ± 0.00	NS
Volume (mm^3) interpolated	1343.36 ± 446.61	1511.67 ± 342.49	**<0.05**
Area (mm^2) Cartilage-Bone boundary	930.03 ± 255.85	906.54 ± 105.55	NS
Lateral cartilage structure of the tibia			
Mean thickness (mm)	1.64 ± 0.49	1.67 ± 0.35	**<0.01**
Maximum thickness (mm)	3.30 ± 0.98	3.38 ± 0.73	**<0.01**
Minimum thickness (mm)	0.31 ± 0.00	0.31 ± 0.00	**<0.01 [as written in journal article]**
Volume (mm^3) interpolated	1706.83 ± 630.84	1739.23 ± 453.24	**<0.05**
Area (mm^2) Cartilage-Bone boundary	896.69 ± 232.44	897.29 ± 165.35	NS

Cartilage thickness of the femur (mean ± SD)

Clinical outcome	Before therapy	After therapy	p value
Mean thickness (mm)	1.62 ± 0.25	1.54 ± 0.21	NS
Maximum thickness (mm)	3.61 ± 0.38	3.50 ± 0.58	NS
Minimum thickness (mm)	0.27 ± 0.11	0.22 ± 0.15	NS
Volume (mm^3) interpolated	9214.30 ± 1862.46	8349.79 ± 1555.34	NS

Key safety findings

Not reported.

Validity and generalisability of the studies

- Only 3 studies in the English language were found suitable for inclusion in the overview.
- There may be more relevant studies available in German.
- The Froböse (2000) study was published in German but we used an English translation of this study to extract the main outcomes.
- One RCT is included in the overview.
- The longest follow-up was 1 year.
- No studies on pulsed electromagnetic fields (PEMFs) were included as it was considered out of remit.
- Two of the studies used the same device and the third one used a different device.

Existing assessments of this procedure

The Osteoarthritis Research Society International (OARSI) guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis were published in 2019. They recommended against the use of electromagnetic therapies interventions for knee OA. [4]

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Platelet-rich plasma injections for knee osteoarthritis. NICE interventional procedures guidance 637 (2019). Available from http://www.nice.org.uk/guidance/IPG637

- Mosaicplasty for symptomatic articular cartilage defects of the knee. NICE interventional procedures guidance 607 (2018). Available from http://www.nice.org.uk/guidance/IPG607

- Joint distraction for knee osteoarthritis without alignment correction. NICE interventional procedures guidance 529 (2015). Available from http://www.nice.org.uk/guidance/IPG529

- Implantation of a shock or load absorber for mild to moderate symptomatic medial knee osteoarthritis. NICE interventional procedures guidance 512 (2015). Available from http://www.nice.org.uk/guidance/IPG512

- Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis. NICE interventional procedures guidance 230 (2007). Available from http://www.nice.org.uk/guidance/IPG230

Technology appraisals

- Autologous chondrocyte implantation using chondrosphere for treating symptomatic articular cartilage defects of the knee. NICE technology appraisal 508 (2018). Available from http://www.nice.org.uk/guidance/TA508
- Autologous chondrocyte implantation for treating symptomatic articular cartilage defects of the knee. NICE technology appraisal 477 (2017). Available from http://www.nice.org.uk/guidance/TA477

NICE guidelines

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

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional 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 professional experts, 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. No Professional expert questionnaires for magnetic resonance therapy for knee osteoarthritis were submitted.

Patient commentators' opinions

NICE's Public Involvement Programme sent questionnaires to patient organisations and NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 1 company who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

The remit of this IPG is restricted to MRT only. NICE considered pulsed electromagnetic fields (PEMFs) out of remit for this guidance.

References

1. Kullich W, Overbeck K and Spiegel H U (2013) One-year-survey with multicenter data of more than 4,500 patients with degenerative rheumatic diseases treated with therapeutic nuclear magnetic resonance. Journal of back and musculoskeletal rehabilitation 26(1): 93-104
2. Goksen N, Calis M, Dogan S et al. (2016) Magnetic resonance therapy for knee osteoarthritis: a randomized, double blind placebo-controlled trial. European journal of physical and rehabilitation medicine 52(4): 431-9
3. Froböse I, Eckey U, Reiser M et al. (2000) Evaluation of the effectiveness of three-dimensional pulsating electromagnetic fields of MultiBioSignalTherapy (MBST ®) on the regeneration of cartilage structures [Evaluation der Effektivität dreidimensionaler pulsierender elektromagnetischer Felder der MultiBioSignalTherapie (MBST®) auf die Regeneration von Knorpelstrukturen]; Orthopaedische Praxis 8/2000, 510–515
4. Bannuru RR, Osani MC, Vaysbrot EE, et al. (2019) OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage. 27(11):1578-1589. doi:10.1016/j.joca.2019.06.011

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	18/08/2020	Issue 8 of 12, August 2020
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	18/08/2020	Issue 8 of 12, August 2020
HTA database (CRD website)	18/08/2020	-
MEDLINE (Ovid)	18/08/2020	1946 to August 17, 2020
MEDLINE In-Process (Ovid) & MEDLINE ePubs ahead of print (Ovid)	18/08/2020	August 17, 2020
EMBASE (Ovid)	18/08/2020	1974 to 2020 August 17

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- 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
- 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.

Literature search strategy

1 Osteoarthritis, Knee/ (20044)
2 exp Knee Joint/ (60472)
3 OA.tw. (29335)
4 ((knee* or patella* or meniscal* or articular* or patellofem*) adj4 (OA or osteoarthrit* or arthros* or cartilag* or degenerat* or diseas* or deteriorat* or injur* or defect*)).tw. (51640)
5 ((cartilage* or joint* or cap*) adj4 (degenerat* or diseas* or deteriorat* or injur* or defect*)).tw. (45374)

6 Gonarthrosis*.tw. (974)
7 (degenerat* adj4 arthriti*).tw. (1676)
8 or/1-7 (151298)
9 nuclear magnetic resonance, biomolecular/ (29086)
10 Magnetic Field Therapy/ (1150)
11 ((magnet* or electromagnet* or "electro-magnet*" or "electro magnet*") adj4 (resonan* or field* or stimulat*) adj4 (therap* or treatment*)).tw. (4660)
12 (magnet* adj4 resonan* adj4 stimulat*).tw. (550)
13 (MBST or MRT or NMRT or TMR or TNMR).tw. (5953)
14 ((magnet* or electromagnet* or "electro-magnet*" or "electro magnet*") adj4 (cartilage or bone* or cell*) adj4 (regenerat* or repair* or regrow* or re-grow* or heal* or rehab* or reconstruct*)).tw. (292)
15 ("NMR Therap*" or NMR-Therap*).tw. (2)
16 (biophysic* adj4 stimul*).tw. (262)
17 or/9-16 (41643)
18 8 and 17 (392)
19 ARTHRO SPIN FLEX.tw. (0)
20 ARTHRO SPIN LIFT.tw. (0)
21 OPEN SYSTEM 700.tw. (0)
22 OPEN SYSTEM 350.tw. (0)
23 MBST PRO MOBILE.tw. (0)
24 or/19-23 (0)
25 18 or 24 (392)
26 animals/ not humans/ (4692605)
27 25 not 26 (331)

Appendix

There were no additional papers identified.