NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of mosaicplasty for symptomatic articular cartilage defects of the knee

Articular cartilage covers the end of the bones in a joint (such as the knee) and stops them rubbing together when you move. It can be damaged because of injury, disease (such as osteochondritis, which is inflammation of the cartilage or bone), or wear and tear. This can cause pain and further damage to the joint, and affect mobility. Mosaicplasty is done by open or keyhole surgery. Healthy cartilage is taken from a donor site at the edge of the joint, which bears less weight, and is inserted into drilled tunnels in the damaged site. The aim is to encourage cartilage healing and produce a more durable joint surface.

Contents

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 specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2017.

Procedure name

- Mosaicplasty for symptomatic articular cartilage defects of the knee

Specialist societies

- British Association for Surgery of the Knee
- Royal College of Surgeons of England.

Description of the procedure

Indications and current treatment

Full thickness cartilage defects of articular surfaces in weight-bearing joints may be limited to the joint surface (chondral) or involve the underlying bone (osteochondral). Common symptoms include pain, catching, locking and swelling, and may lead to further degenerative changes within the joint. These defects usually occur after direct trauma, but can also occur in avascular necrosis, osteochondritis dissecans and a variety of cartilage disorders.

There is no uniform approach to managing cartilage defects in the knee. Treatment options depend on the size of the defect and its location. There are 2 main categories of procedure: those intended primarily for symptom relief and those that also try to re-establish the articular surface. Interventions that aim to re-establish the articular surface include marrow stimulation techniques (such as abrasion arthroplasty, Pridie drilling and microfracture), mosaicplasty (also known as osteochondral transplantation) and autologous chondrocyte implantation (in which chondrocytes harvested from the knee are cultured and implanted into the damaged cartilage). Interventions that aim to relieve symptoms include knee washout (lavage) with or without debridement, osteotomy and knee replacement.

What the procedure involves

Mosaicplasty (also called osteochondral autologous transfer mosaicplasty - OATM) is a technique for creating an osteochondral autograft. Small cylindrical osteochondral plugs are harvested from the periphery of the patellofemoral area (because it bears less weight) and inserted into drilled tunnels in the affected

weight-bearing part of the knee joint. The procedure is done in a single sitting, commonly by open surgery but sometimes arthroscopically when perpendicular access to the harvesting and implantation sites is feasible. The harvesting and implantation process is repeated until about 70% of the defective area is filled, with minimal spacing between plugs. The number and size of plugs used may vary depending on lesion size and mosaicplasty technique. A drain is usually needed postoperatively and the patient is advised not to weight bear for 4 to 8 weeks depending on the size and location of the treated defect. Passive mobilisation after surgery is done for 2 to 4 weeks, progressing to active mobilisation and physiotherapy that is continued for several months.

Outcome measures

Outerbridge Classification grading system of chondral and osteochondral injuries of the knee:

- **Grade 0**: normal cartilage
- **Grade I**: cartilage with softening and swelling
- **Grade II**: a partial-thickness defect with fissures on the surface that do not reach subchondral bone or exceed 1.5 cm in diameter
- **Grade III**: fissuring to the level of subchondral bone in an area with a diameter more than 1.5 cm
- **Grade IV**: exposed subchondral bone.

Hospital for Special Surgery (HSS) Score

Score for classification of patient functional status after knee surgery:

- **90 to 100:** excellent
- **70-89:** good
- **50-69:** fair
- **less than 50:** poor.

Lysholm knee scale (0 to 100)

Originally designed to assess ligament injuries of the knee but later used to assess chondral injuries of the knee, this outcome measure contains 8 domains: limp, locking, pain, stair climbing, support, instability, swelling, and squatting. A score of 0 to 100 is calculated:

- 95 to 100: excellent result
- 84 to 94: good result
- 65 to 83: fair result
- less than 65: poor result.

Grading the Tegner Lysholm Knee Scoring Scale (0 to 100 or 0 to 10)

- Less than 65: poor
- 65-83: fair
- 84-90: good
- over 90: excellent.

The Tegner activity level scale is used with the Lysholm knee scale. It was originally used in patients with anterior cruciate ligament (ACL) injury. It is a graduated list of activities of daily living, recreation and competitive sports. The patient is asked to select the level of participation that best describes their current level of activity and that before injury. It was developed to complement the Lysholm knee scale after noticing that limitations in function scores in that scale may be masked by a decrease in activity level.

Marx Activity Rating Scale (MARS) (0 to 10)
MARS is a measure of the types of functional activities associated with high-level knee function; a higher score indicates more functional demand on the knee joint and potentially a higher risk of injury. Each item is scored on a 5-point ordinal scale ranging from 0 (less than 1 time in a month) to 4 (4 or more times in a week), and the total scale score is obtained by adding up the individual items' scores (range, 0 to 16).

International Cartilage Repair Society (ICRS) evaluation system
This system is used to evaluate cartilage repair macroscopically (possible interpretation 0 to 12)
0 to 3 – severely abnormal cartilages
4 to 7 – abnormal cartilages
8 to 11 – nearly normal cartilages
12 – normal looking cartilages.

The ICRS score is the sum of 3 subscores (0 to 4 points each):
- percentage survival of initially grafted surface
- integration with surrounding cartilage
- macroscopic appearance.

International Knee Documentation Committee (IKDC) (0 to 100)
This is a knee-specific patient-reported outcome measure questionnaire. The questionnaire looks at 3 categories: symptoms, sports activity and knee function. Scores are obtained by adding up the individual items, then transforming the total to a scaled 0 to 100 range. The final number result is interpreted as a measure of function, with higher scores representing higher levels of function.

Knee Outcome Survey (KOS)
The KOS is a patient self-report survey that includes an Activities of Daily Living Scale (ADLS) and a Sports Activity Scale (SAS). The ADLS is a 14-item questionnaire that asks patients about how their knee symptoms effect their ability to do general daily activities (6 items) as well as how their knee condition affects their ability to do specific functional tasks (8 items). Higher percentages reflect higher levels of functional ability. The SAS is an 11-item scale that asks patients about how their symptoms affect their ability to do sports and recreational activities (7 items) as well as how their knee condition effects their ability to do specific sports-related activities such as straight running, jumping

and landing, quick stopping and starting, cutting and pivoting (4 items). Higher percentage ratings reflect higher levels of sports and recreational function. This scale was developed to assess higher levels of physical function for patients with knee pathology.

Modified O'Driscoll Scale (MODS) (range 0 to 21)
This scale assesses the level of integration of the repair tissue with its surroundings, including 4 major categories: nature of the predominant tissue; structural characteristics; freedom from cellular changes of degeneration; and freedom from degenerative changes in adjacent cartilage. A higher score implies better cartilage repair.

Kellgren-Lawrence system
This is a method for classification of the severity of knee osteoarthritis using 5 grades:
- **Grade 0**: no radiographic features of osteoarthritis are present
- **Grade 1**: doubtful joint space narrowing and possible osteophytic lipping
- **Grade 2**: definite osteophytes and possible joint space narrowing on anteroposterior weight-bearing radiograph
- **Grade 3**: multiple osteophytes, definite joint space narrowing, sclerosis, possible bony deformity
- **Grade 4**: large osteophytes, marked joint space narrowing, severe sclerosis and definite bony deformity

Hughston Clinic subjective knee questionnaire
This is a 28-item knee-specific questionnaire that asks about the patients' perception of their knee condition 10 (See Appendix I). Each item of the questionnaire is scored on 10-cm visual analogue scale with a descriptor on each end of the horizontal line.

Magnetic resonance observation of cartilage repair tissue (MOCART)
The MOCART scoring system is an evaluation method for assessing repaired cartilage that looks at: degree of defect repair and defect filling; integration with the border zone; quality of repaired tissue surface; adhesion; and synovitis. It is useful for long-term follow-up after knee cartilage repair.

Efficacy summary

Clinical outcomes

In a systematic review (SR) including 6 randomised controlled trials (RCTs) and 3 non-randomised controlled studies (NRCS) with a total of 607 patients, the outcomes of several surgical procedures to treat knee cartilage defects were compared. The studies were reported on individually. In an RCT of 50 patients, clinical and functional outcomes were better in athletes younger than 30 years who had OATM than in older patients (p=0.008) at 4-year follow-up. In an NRCS of 70 patients, there was no statistically significantly difference in functional outcomes or postoperative MRI evaluations between patients who had OATM, autologous chondrocyte implantation (ACI) or microfracture (MF) at 3-year follow-up. In an RCT of 25 patients, there was no statistically significantly difference between OATM and MF in patient-reported outcomes, muscle strength or radiological outcomes at 10-year follow-up; however, there were more reoperations in the MF group (p value not reported). In an NRCS of 40 patients, clinical outcomes at 2-year follow-up were better in patients who had OATM than in those who had ACI (p value not reported). In an RCT of 100 patients, there was more normal cartilage on arthroscopic evaluation and improved clinical scores in patients who had OATM than in patients who had ACI at 18-month follow-up (p value not reported). In another RCT of 100 patients, rate of failure at 10-year follow-up was greater in patients who had OATM (5% [23/42]) than in those who had ACI (17% [10/58], p value not reported). An RCT of 60 patients who had OATM reported improved HSS scores at 3-year follow-up (from a mean of 77 preoperatively to 91, p value not reported). In the RCT of 50 patients, clinical outcomes in paediatric patients with cartilage lesions greater than 3 cm^2 who had OATM were worse than those in patients with smaller lesions (p value not reported). Similarly, in another RCT of 60 patients, there was a higher rate of return to sport in patients who had OATM for lesion smaller than 2 cm^2 than in patients treated for larger lesions (p value not reported). The same RCT found no difference in clinical outcome between patients who had OATM for lesions of the medial or lateral femoral condyle.[1]

Macroscopic and microscopic cartilage outcomes

In the RCT of 60 patients and 3-year follow-up included in the SR of 607 patients, normal appearing cartilage on visual inspection was statistically significantly more frequent in patients who had OATM than in patients who had MF (p=0.004). In the RCT of 50 patients included in the same SR, cartilage deterioration was less frequent in patients who had OATM than in those who had MF at the 4-year follow-up (p value not reported). In the same RCTs of 60 patients and 3-year follow-up,), ICRS scores improved from a mean of 51 preoperatively to 75 at 37-month follow-up. Similarly, in 1 RCT (n=50), ICRS score improved from a mean of 51 preoperatively to 92 at 1-year follow-up, which then decreased to 83 at 4-year follow-up. The other RCT of 60 patients from the same SR found that ICRS

scores in patients who had OATM was statistically significantly improved from a mean preoperative value of 61 to 93 at 10-year follow-up ($p<0.01$).[1]

In a network meta-analysis of 19 RCTs (including a total of 855 patients), patients who had OATM were statistically significantly more likely to generate hyaline cartilage than patients who had MF (odds ratio [OR] 16.13, 95% confidence interval [CI] 2.8 to 92.91) or who had first-generation (using autologous periosteum flap to cover the cartilage defect) ACI (OR 6.42, 95% CI 1.09 to 37.93) at a follow-up of 2 years to 10 years.[2]

In 1 case series of 26 patients in an SR of 10 studies (including a total of 610 patients), there was a statistically significantly better IKDC score in patients who had OATM with only 1 plug than in patients treated with 4 plugs (85 compared with 50; $p<0.05$). Conversely, in a case series of 24 patients in the same SR, the number of plugs did not statistically significantly affect ICRS scores or failure rate ($p=0.42$) at 10-year follow-up.[3]

In an RCT of 55 patients, 47 patients had histology samples assessed using the O'Driscoll score (range 0 to 21, with a higher score meaning better cartilage repair). Mean score overall was statistically significantly better in patients who had OATM (18.5±2.5, range 14 to 21) than in patients who had ACI using Cartipatch (15.1±3.7, range 10 to 19); there was 3.3-point difference at 2-year follow-up ($p=0.02$). However, the O'Driscoll score was not statistically significantly different between groups with defects smaller than 3.5 cm^2 ($p=0.43$) or greater or equal to 3.5 cm^2 ($p=0.28$).[5]

In a case series of 142 patients who had OATM, there were 35 arthroscopies done at follow-up and graft integration was considered complete in 31% (11/35).[6]

In a case series of 534 patients, good joint congruity was maintained in 95% (21/22) of patients who were non-weight bearing for 4 weeks after surgery compare with and 100% (46/46) of patients who were weight bearing as tolerated. There was no statistically significantly difference in the frequency of repair of adjacent defects between non-weight bearing and weight-bearing as tolerated groups ($p=0.94$). Mean total ICRS macroscopic cartilage repair score difference (0.13, 95% CI -0.605 to 0.345) was higher in the weight-bearing as tolerated group than in the non-weight-bearing group, but this did not reach statistical significance ($p=0.71$). There was no statistically significantly difference in pain resolution between one of the non-weight-bearing groups (A) and the weight-bearing as tolerated group ($p=0.25$).[7]

Radiographic outcomes

In the SR of 607 patients, 4 out of 9 studies reported radiographic outcomes of cartilage repair surgery. In the RCT of 60 patients and 30-year follow-up, there were no arthritic changes on plain radiographs in patients who had OATM before surgery or at 3-year follow-up, and incorporation of osseous components was

complete in 92% (23/25) of patients who had MRI scans. In the other RCT of 60 patients, 25% (7/28) of patients had evidence of Kellgren-Lawrence grade I osteoarthritis but this did not influence the final ICRS score (p=0.094). Joint surface congruence was restored in 96% (24/25) of the patients who had OATM at 10-year follow-up. In the RCT of 50 patients, 100% (21/21) of osteochondral transplants had completely healed without any degenerative changes on MRI in 21 out of 25 paediatric patients who had OATM. In the RCT of 25 patients, Kellgren-Lawrence scores greater than II were present in radiographs in 17% (2/12) of patients who had OATM. One of these patients had osteoarthritis in the contralateral knee.[1]

In the SR of 610 patients, the included case series of 26 patients reported a statistically significantly worse postoperative Kellgren-Lawrence score in patients who had OATM with 3 or more donor plugs compared with those with 1 or 2 plugs (p=0.044).[3]

In the case series of 142 patients, Hughston radiological score of 3 or 4 were reported in 80% (114/142) of patients at 8-year follow-up. In the same case series, a modified 11-point MOCART (in which a higher score means better cartilage repair) score was created based on MRI examinations (n=80) and mean score was 7 (range 4 to 10). Also, patellofemoral osteoarthritis was present in 13% (18/142) of patients, at 8-year follow-up.[6]

Activity levels and quality of life

In the NRCS of 100 patients in the SR of 607 patients, the level of activity post OATM and concomitant ACL repair was assessed using the Tegner score; preoperative scores decreased from 7.3 to 7.1 at 3-year follow-up. Nonetheless, the delta decline (0.2) was smaller for patients who had OATM compared with the patients who had MF and debridement. The same NRCS reported an improvement in IKDC score from mean preoperative values of 46 to 88 in patients who had OATM, at 3-year follow-up. In the RCT of 25 patients, level of function in patients who had OATM was assessed using the Lysholm score; mean scores improved from 49 preoperatively to 63 at 10-year follow-up. In the NRCS of 70 patients, Lysholm scores increased from 53 to 85, Tegner scores from 2.7 to 5.4 and HSS scores from 79 to 88 at 5-year follow-up.[1]

In the SR of 10 studies (n=610), mean time to weight bearing in patients who had OATM (n=221) was 4.7 weeks and mean time to full activity was 13.7 weeks. The same SR included 5 studies of 119 patients treated by OATM that did not find statistically significantly difference in mean Tegner scores from preoperative to postoperative values (0.76, 95% CI -0.83 to 2.36, p=0.35). IKDC scores reported in 3 studies (n=70) statistically significantly improved by 42.4% (95% CI 31.8 to 53.1, p<0.001) from baseline assessment. Lysholm scores reported in 3 studies (n=104) also statistically significantly improved by 21.1 (95% CI 12.2 to 30, p<0.01) from baseline assessment.[3]

In the RCT of 55 patients mean IKCD score improvement was statistically significantly higher in patients who had OATM (44.3±15.2) in comparison to patients who had ACI (31.8±20.8), mean difference 12.6, p=0.028, at 2-year follow-up. The IKCD score was not influenced by BMI (p=0.83), time from onset to index surgery (p=0.61), mode of symptom onset (p=0.79), cause of injury (p=0.45), sports level (p=0.79), limb alignment (p=0.09), surgical knee history (p=0.67) and number and size of the plugs used (p=0.52).[5]

In the case series of 142 patients who had OATM, most patients (82%) were very satisfied or satisfied at 8-year follow-up. There was also a statistically significant improvement in ICRS scores (p<0.001), IKDC function (p<0.001) and Hughston scores (p<0.001) at follow-up. The delay from injury to treatment by OATM was correlated with statistically significantly worse IKDC scores (p=0.03) and a greater delay between the surgery and follow-up was related with statistically significantly lower IKDC scores (p<0.001). A Hughston score of 4 was statistically significantly more frequent in patients who had OATS with injuries caused by osteochondritis than in patients with chondral fracture (p=0.001). There was also a statistically significantly better objective IKDC scores in men (p=0.009). Patients who had OATM for deeper lesions (depth of IV in the ICRS score) had a better outcome than patients with more superficial lesions (grade II and III). Also, patients with medial condyle defects had better ICRS clinical and Hughston scores than patients with lateral condyle or patellofemoral compartment defects (p=0.009) at 8-year follow-up. Hughston scores of 3 or 4 were statistically significantly more frequently in patients with defects smaller than 2 cm^2 than in patients with defects between 2 cm^2 and 4 cm^2 (p=0.05) at 8-year follow-up.[6]

In an NRCS of 96 patients, knee function assessed by the KOS–ADLS score and IKDC score improved statistically significantly from baseline to 1, 2, 3 and 5 years postoperatively in both OATM and MF groups (p<0.01 for all). The scores did not differ statistically significantly between the groups at any point. Knee function assessed by the MARS was statistically significantly better in the OATM group than in the MF group at 2 years (p=0.001), 3 years (p=0.03) and 5 years (p=0.02) postoperatively. Quality of life was statistically significantly improved from baseline assessment in patients who had OATM or MF (p<0.01) at 1-, 2-, 3- and 5-year follow-up.[8]

Return to sport

In 2 RCTS (n=110) included in the SR of 607 patients, return to play in patients who had OATM happened at 6.5 months. In the RCT of 60 patients and 10-year follow-up, there was a higher return to play rate and maintenance of sport at the preinjury level in patients who had OATM than in patients who had MF. In the same study, maintaining preinjury levels of sport was more common at 4-year follow-up in athletes younger than 30 years who had OATM than in those who were older at the time of the procedure. In the paediatric population, 84% of the patients were at preinjury activity level 12 months postoperatively, with 81% of

patients continuing to participate in the same level of activity at 4-year follow-up. In the NRCS of 100 patients, the average return to play in patients who had OATS and ACL reconstruction was 10 months.[1]

In the SR of 10 studies (n=610), 85% (97/114) of patients who had OATM returned to sport in the 3 studies that reported on this outcome.[3]

Treatment failure and reoperation

In the RCT of 100 patients and 1-year follow-up in the SR of 607 patients, cartilage lesions of the patella were unsuccessfully treated in 1% (7/100) patients who had OATM. In the NRCS of 70 patients, 5% (1/25) of patients needed arthroscopic reoperation because of a limited range of motion caused by a prominent osteochondral plug. In the RCT of 25 patients, the reoperation rate in patients who had OATM was 36% (5/14); 4 procedures were diagnostic arthroscopies or debridement and 1 was an opening wedge osteotomy. In the RCT of 100 patients and 10-year follow-up, reoperation rate was 23% (23/100); 9 were ACIs, 5 were unknown, 3 were matrix-induced chondrocyte implantations, 3 were unicondylar knee replacements, 1 was a patelofemoral joint replacement, 1 was a combined medial patellofemoral joint replacement and 1 was a total knee arthroplasty. Mean time from the index procedure to revision surgery was 4 years (range 1 year to 9 years).[1]

In the network meta-analysis of 855 patients, there was no statistically significantly difference in reoperation rates at 2-year follow-up between OATM, MF or ACI. However, reoperation rates were statistically significantly lower in patients who had OATM compared with MF (OR 0.03, 95% CI 0.00 to 0.49) and compared with ACI (OR 0.03, 95% CI 0.00 to 0.59) at the 5-year follow-up. Reoperation rates at 10-year follow-up were higher in patients who had OATM compared with ACI (OR 5.81, 95% CI 2.33 to 14.47).[2]

In the SR of 10 studies (n=610), mean OATM treatment failure was 28% and mean reoperation rate was 19%. There were 112 reoperations reported in 7 of the 10 studies: 54% were surgical debridement because of symptoms in the same joint, 28% were revision cartilage surgeries, 14% were knee arthroplasties, 3% were high tibial or distal femoral osteotomies, and 2% were surgeries unrelated to the original cartilage defect. Factors that had a statistically significantly positive correlation with OATM failure were: age at the time of surgery ($r=0.775$, $p<0.01$), previous surgery ($r=-0.689$, $p<0.01$) and defect size ($r=0.952$, $p<0.01$). Failure rate had a statistically significantly negative correlation with concomitant surgical procedures ($r=-0.663$, $p<0.01$). Age at the time of surgery had a statistically significantly positive correlation with reoperation rate ($r=0.896$, $p<0.01$) and so did defect size ($r=0.863$, $p<0.01$). Reoperation rate had a statistically significantly negative correlation with concomitant surgical procedures ($r=-0.790$, $p<0.01$).[3]

In the case series of 534, in patients who had OATM, reoperations were statistically significantly less likely in the weight-bearing as tolerated group than in the non-weight-bearing group ($p<0.001$).[7]

Safety summary

Infection

Deep infection was reported in less than 1% (2/303) of patients who had OATM in a case series included in the SR of 610 patients, at 10-year follow-up.[3]

There were 4 episodes of intra-articular effusion in 8% (2/25) of patients who had OATM compared with 7 episode in 30% (6/30) of patients who had ACI using Cartipatch in the RCT of 55 patients, at 2-year follow-up. Popliteal cyst occurred in 1 of 25 patients who had OATM and in 1/ of 7 patients who had ACI using Cartipatch in the same RCT.[5]

Sepsis was reported in 1 of 142 patients in a case series of patients who had OATM, at 8-year follow-up.[6]

Infection was statistically significantly more frequent in the weight-bearing as tolerated group (2 of 437 patients) than in the non-weight-bearing groups (0 patients, $p<0.001$) in the case series of 534 patients who had OATM at 32 to 39-month follow-up.[7]

Deep vein thrombosis and pulmonary embolus

Venous thrombosis was reported in 1% (3/303) of patients who had OATM in a case series included in the SR of 610 patients, at 10-year follow-up.[3]

Deep vein thrombosis was statistically significantly less frequent in the weight-bearing as tolerated group (1% [3/437]) than in the non-weight-bearing group with ACL repair (3% [1/29]) or without ACL repair (3% [2/68], $p<0.001$) in the case series of 534 patients who had OATM at 32- to 39-month follow-up. Also, pulmonary embolism was statistically significantly less frequent in the weight-bearing as tolerated group (0%) than in the non-weight-bearing group without ACL repair (2% [1/68], $p<0.001$).[7]

Morbidity related to the donor site

In an SR of 21 studies (including a total of 1,726 patients), which reported on donor site morbidity in patients who had OATM, persistent patellofemoral pain was reported in 4% (1/25) of patients in an included RCT with 2-year follow-up. Moderate and severe donor site disturbances were reported in 3% (29/967) of patients in a case series (minimum 12-month follow-up). Patellofemoral complaints occurred in 5% (15/303) of patients in a case series with 10-year follow-up. Minor postoperative effusion occurred in 1 patient in a case series of

42, at 37-month follow-up. Crepitation was reported in 36% (15/42) of patients of the same case series. Retropatellar crepitus happened in 92% (12/13) of patients in a case series, at 49-month follow-up. Patellar chondropathy occurred in 22% (4/18) patients and joint effusion in 38% (7/18) in a case series, at the 27-month follow-up. Discomfort in the back of the knee during stair climbing or kneeling was reported in 13% (2/16) patients in a case series with 14 months of follow-up. Osteoarthritis occurred in 1 patient in the case series of 17 at 12-month follow-up.[4]

Persistent patella-femoral pain occurred in 1 of 25 patients who had OATM compared with 0 of 30 patients who had ACI using Cartipatch in the RCT of 55 patients, at 2-year follow-up. Complex regional pain syndrome was reported in 0 of 25 patients who had OATM compared with 1 of 30 patients.[5]

Haematoma

Haematoma occurred in 1 of 25 patients who had OATM compared with 2 of 30 patients who had ACI using Cartipatch in the RCT of 55 patients, at 2-year follow-up[5].

Haemarthrosis was reported in 4% (6/142) of patients in the case series of 142 patients, at 8-year follow-up.[6]

Haemarthrosis was statistically significantly more frequent in the weight-bearing as tolerated group (less than 1% [1/437]) than in the non-weight-bearing groups (0%, p<0.001) in the case series of 534 patients who had OATM at 32- to 39-month follow-up.[7]

Other

A total complication rate of 13% (19/142) was reported in the case series of 142 patients who had OATM, at 8-year follow-up. Complex regional pain syndrome was reported in 1 of 42 patients at 8-year follow-up.[6]

Arthrofibrosis was statistically significantly less frequent in the weight-bearing as tolerated group (0%) than in the non-weight-bearing group with ACL repair (7% [2/29]) or without ACL repair (5% [3/68], p<0.001) in the case series of 534 patients who had OATM, at 32- to 39-month follow-up.[7]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers 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, specialist advisers listed

no new anecdotal adverse events. They considered that the following was a theoretical adverse event: iatrogenic fracture during harvesting.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to mosaicplasty for symptomatic articular cartilage defects of the knee. The following databases were searched, covering the period from their start to 11 January 2017: 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 in which no clinical outcomes were reported, or in which 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 full thickness symptomatic knee cartilage defects.
Intervention/test	Mosaicplasty for symptomatic articular cartilage defects of the knee.
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 approximately 3127 patients from 1 network meta-analysis[2], 3 SR[1, 2, 4], 1 RCT[5], 2 case series[5, 6] and 1 NRCS[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 mosaicplasty for symptomatic articular cartilage defects of the knee

Study 1 Lynch S (2015)

Details

Study type	**Systematic review**
Country	US
Recruitment period	Databases searched between 1950 and 2013
Study population and number	9 studies (6 RCTs, 3 NRCS), 607 patients
Age and sex	14 to 33 years
Patient selection criteria	Inclusion criteria: - Paediatric or adult patients with grade 3 or 4 cartilage injuries of the knee - Study sample size ≥25 patients - Follow-up of at least 12 months - Comparing OATM with another treatment modality - RCT and cohort studies - English language
Technique	Full thickness cartilage defects of the knee were treated by MF, OATM, ACI-C or ACI-P.
Follow-up	**1 to 10 years**
Conflict of interest/source of funding	The author reported having received funding from Arthrosurface, Stryker Smith & Nephew, Zimmer, Arthrex and DJO.

Analysis

Follow-up issues: None

Study design issues: Two authors have independently searched the literature. The literature search was systematic and comprehensive following a PRISMA guideline.

Main outcomes were patient reported and functional outcomes including effect on lesion size, return to sport and sport function, radiographic outcomes and reoperation rates.

Study population issues:

Author	Study design	comparators	n, follow-up	Lesion size (cm^2)
Bentley 2003	RCT	OATM, ACI-P, ACI-C	100, 1 year	4.66 (1 to 12.2)
Bentley 2012	RCT	OATM, ACI-P, ACI-C	100, 10 years	4.66 (1 to 12.2)
Gudas 2005	RCT	OATM, MF	60, 3 years	2.8 (1 to 4)
Gudas 2009	RCT	OATM, MF	50, 4 years	3.2
Gudas 2012	RCT	OATM, MF	60, 10 years	2.8 (1 to 4)
Ulstein 2014	RCT	OATM, MF	25, 10 years	MF 2.6 (2 to 5.2), OATM (32 to 6)
Gudas 2013	NRCS	OATM, MF	100, 36 months	2.6 (2 to 4)
Horas 2003	NRCS	OATM, ACI-P	40, 2 years	3.75 (3.2 to 5.6)
Lim 2012	NRCS	OATM, MF, ACI	70, 6 years	2.7 (1 to 4)

Is studies by Ulstein 2014, Gudas 2013 and Lim 2012 patients were allowed to partially weight bear immediately after surgery, in the remaining this was allowed 2 to 4 weeks post-operatively. In the studies by Bentley patients were allowed to full weight bear 1 day after surgery, whilst a 6 to 12-week period was used by other authors.

Some patients included in Gudas 2013 had anterior cruciate ligament repair done at the time of cartilage repair procedures. Gudas 2009 reports on a paediatric population.

Other issues: The studies by Bentley 2003, Bentley 2012, Gudas 2005, Gudas 2009, Gudas 2012, Horas 2003 and Ulstein 2014 were also reported by paper 2 in table 2. The studies by Bentley 2012, Gudas 2012 and Ulstein 2014 were also reported by paper 3 in table 2.

Key efficacy and safety findings

Efficacy	Safety
n= 607 patients, 9 trials (6 RCTs, 3 NRCS) **Clinical results** **OATM vs MF** Gudas 2005: Clinical results of OATM superior to MF (p<0.01), and more normal appearing cartilage on visual inspection (p=0.004) Gudas 2009: OAT superior to MF with deterioration present in the MF group at the 4-year follow-up Gudas 2009: athletes younger than 30 years had better clinical and functional outcomes that older patients (p=0.008), at 4-year follow-up Lim 2012: No difference in functional outcomes or postoperative MRI evaluations between OATM, ACI or MF, at 3-year follow-up Ulstein 2014: no difference between OATM and MF in patient reported outcomes, muscle strength or radiological outcomes however there were more reoperations in the MF group **OATM vs ACI** Horas 2003: improved clinical outcomes favouring the OATM group when compared with ACI. Bentley 2003: more normal cartilage on arthroscopic evaluation in the ACI group, with improved clinical scores at 18-month follow-up Bentley 2012: greater rate of OATM failure (5% [23/42]) in comparison to ACI (17% [10/58]) at the 10-year follow-up **Lesion size** Gudas 2009: worse outcomes in paediatric patients with lesions greater than 3 cm^2 treated by OATM Gudas 2012: Lesion size less than 2 cm^2 was associated with a significantly higher rate of return to sport compared with larger lesions treated by OATM **Lesion location**: there was no difference in clinical outcome between locations of the lesion either on medial or lateral femoral condyle. Bentley 2003: Failure of 7 patellar lesions treated by OATM, at 2-year follow-up. **Outcomes measures** **HSS score** (0 = lowest level of function, 100 = better level of function) Gudas 2005 – score improved from a mean of 77 preoperatively to 91 at 37-month follow-up **ICRS score** (0 = severely abnormal cartilage, 100 = normal looking cartilage) Gudas 2005: ICRS score improved from a mean of 51 preoperatively to 75, at 37-month follow-up Gudas 2009: ICRS score improved from a mean of 51 preoperatively to 92, at 1-year follow-up and then decreased to 83, at 4-year follow-up Gudas 2012: mean preoperative ICRS score was 61 improving to 93, at 10-year follow-up (p<0.01) **Tegner score** (0 = lowest level of function, 10 = better level of function) Gudas 2013: OATM-ACL Tegner score was 7.3 preoperatively and decreased to 7.1 at 3-year follow-up. The delta decline (0.2) was smaller for the OATM group compared with the MF and debridement groups. **IKDC subjective score** (0 = lowest level of function, 100 = better level of function) Gudas 2012: mean IKDC score preoperative score 46 increased to 88 in patients treated by OATM, at 3-year follow-up. **Lysholm score** (0 = lowest level of function, 10 = better level of function) Ulstein 2014: improvement in mean Lysholm scores from 49 preoperatively to 63 at 10-year follow-up Lim 2012: increase in Lysholm score from 53 to 85, Tegner scores from 2.7 to 5.4 and HSS scores from 79 to 88, at 5-year follow-up. **Return to sport** Gudas 2009 and Gudas 2012: patients treated by OATM could return to play at 6.5 months.	

Gudas 2012: OATM associated to higher return to play and maintenance of sport at the preinjury level when compared with MF, at the 10-year follow-up. Gudas 2012: athletes younger than 30 years treated by OATM were more likely to maintain their preinjury levels compared with those who were older at the time of the procedure. In the paediatric population 84% of the patients achieved the preinjury activity level at 12 months postoperatively, with 81% of patients continuing to participate in the same level of activity at 4-year follow-up. Gudas 2013: In the OATS/ACL, reconstruction group the average return to play was 10 months. **Radiographic outcomes** (reported by 4 of 9 articles) Gudas 2005: no arthritic changes on plain radiographs before surgery or at 3-year follow-up. Incorporation of osseous components was complete in 92% (23/25) of patients that had MRI scans. Gudas 2012: there were 25% (7/28) of patients with evidence of Kellgren-Lawrence grade I osteoarthritis but this did not influence the final ICRS score (p=0.094). Joint surface congruence was also fund to be restored in 96% (24/25) Gudas 2009: (MRI was done in 21 out of 25 paediatric patients) – 100% (21/21) osteochondral transplants had completely healed without any degenerative changes. Ulstein 2014: Kellgren-Lawrence scores greater than II were present in radiographs in 17% (2/12) patients treated by OATM. One of these patients had osteoarthritis in the contralateral knee. **Reoperation** (reported in 3 of 9 studies) Lim 2012: 5% (1/25) of patients required reoperation due to limited range of motion requiring secondary arthroscopy, this was caused by a prominent osteochondral plug Ulstein 2014: 36% (5/14) patients, 4 procedures were diagnostic arthroscopies or debridement and 1 was an opening wedge osteotomy. Bentley 2012: 23% (23/100) reoperations: 9 ACIs, 5 unknown, 3 matrix-induced chondrocyte implantations, 3 unicondylar knee replacements, 1 patelofemoral joint replacement, 1 combined medial patellofemoral joint replacement and 1 total knee arthroplasty. Mean time from the index procedure to revision surgery was 4 years (range 1 to 9)	
Abbreviations used: ACI-C, autologous chondrocyte implantation – collagen cover; ACL, anterior cruciate ligament; ACI-P, autologous chondrocyte implantation – periosteal cover; HSS, hospital for special surgery score; IKDC, International knee Documentation Committee; NRCS, non-randomised comparative study; MF, microfracture; MRI, magnetic resonance imaging; OATM, osteochondral autograft transfer mosaicplasty; PRISMA, preferred reporting items for systematic reviews and meta-analysis; RCT, randomised control trial.	

Study 2 Riboh JC (2016)

Details

Study type	**Network Meta-analysis**
Country	US
Recruitment period	Databases were searched until 2016
Study population and number	19 RCTs, 855 patients (7 RCTS comparing OAT to an alternative intervention)
Age and sex	15 to 39 years
Patient selection criteria	Inclusion criteria: Patients of all ages who had symptomatic articular cartilage defects of the knee, including femoral condyles, trochlea and patella treated in a RCT comparing 2 or more surgical cartilage restoration technique. Exclusion criteria: prior cartilage restoration procedures other than MF, multiple simultaneous cartilage restauration procedures other than that MF, multiple simultaneous cartilage restoration procedure and less than 12-month follow-up.
Technique	Patients were included in RCTS comparing the use 2 or more of the following: MF, augmented MF, ACI with periostal or collagen patch, matrix induced chondrocyte implantation, osteochondral allograft or OAT/mosaicplasty.
Follow-up	**2 to 10 years**
Conflict of interest/source of funding	The authors declared having received personal fees and research support from manufacturers of surgical orthopaedic equipment.

Analysis

Follow-up issues: None.

Study design issues: Bayesian network meta-analysis. The literature search was systematic and comprehensive following a PRISMA guideline.

A separate analysis was done for each outcome. A loop specific approach was used to compare direct and indirect estimates of treatment effects for all closed triangular and quadrangular loops within the network. The difference between direct and indirect estimates is termed inconsistency factor (IF). For categorical variables the IF is a ratio of odds ratios. For continuous variables the IF is a difference of mean differences. The loop was considered inconsistent if the 95% CI excluded the null value.

Study population issues: Minimal heterogeneity was seen in the effect modifiers and only the Lysholm data had statistical inconsistency. Chondral lesions ranged from 2.7 to 6.1 $cm^{2.}$

Included RCTs

Author	Comparators	n, follow-up
Bentley 2003	ACI vs OAT	100, 19 months
Bentley 2012	ACI vs OAT	100, 120 months
Gudas 2005	MF vs OAT	57, 37 months
Gudas 2009	MF vs OAT	47, 50.4 months
Gudas 2012	MF vs OAT	29, 120 months
Horas 2003	ACI vs OAT	40, 24 months
Ulstein 2014	MF vs OAT	25, 118 months

Other issues: The studies by Bentley 2003, Bentley 2012, Gudas 2005, Gudas 2009, Gudas 2012, Horas 2003 and Ulstein 2014 were reported by paper 1 in table 2. The studies by Bentley 2012, Gudas 2012 and Ulstein 2014 were also reported by paper 3 in table 2.

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Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>n=855 (398 patients in 7 OAT trials)

<table>
<tr><td></td><td></td></tr>
<tr><td colspan="2">Reoperation rates</td></tr>
<tr><td>2 years</td><td>Not statistically significantly differences between treatments</td></tr>
<tr><td rowspan="2">5 years</td><td>OAT vs MF: OR 0.03, 95% CI 0.00 to 0.49 [favours OAT]</td></tr>
<tr><td>OAT vs ACI: OR 0.03, 95% CI 0.00 to 0.59 [favours OAT]</td></tr>
<tr><td rowspan="2">10 years</td><td>OAT vs ACI: OR 5.81, 95% CI 2.33 to 14.47 [favours ACI]</td></tr>
<tr><td>MF vs ACI: OR 17.3, 95% CI 4.43 to 67.52 [favours ACI]</td></tr>
<tr><td colspan="2">Likelihood of generating hyaline cartilage</td></tr>
<tr><td colspan="2">OAT vs MF: OR: 16.13, 95% CI 2.8 to 92.91 [favours OAT]</td></tr>
<tr><td colspan="2">OAT vs ACI: OR 6.42, 95% CI 1.09 to 37.93 [favours OAT]</td></tr>
<tr><td colspan="2">MF vs second generation ACI: OR: 0.13, 95% CI 0.02 to 0.85 [favours ACI]</td></tr>
<tr><td colspan="2">Hypertrophy of the cartilage graft</td></tr>
<tr><td colspan="2">MF vs first generation ACI: OR 0.38, 85% CI 0.17 to 0.82 [favours MX]</td></tr>
<tr><td colspan="2">Second generation ACI vs first generation ACI: OR 0.12, 95% CI 0.02 to 0.59 [favours second generation ACI]</td></tr>
<tr><td colspan="2">MACI vs first generation ACI: OR 6.42, 95% CI 1.09 to 37.93 [favours MACI]</td></tr>
<tr><td colspan="2">Lysholm score or Tegner scores</td></tr>
<tr><td colspan="2">No statistically significantly difference between comparators.</td></tr>
</table>
</td><td>None</td></tr>
<tr><td colspan="2">Abbreviations used: ACI, autologous chondrocyte implantation; CI, confidence interval; MACI, matrix-induced chondrocyte implantation; MF, microfracture; OATM, osteochondral autograft transfer mosaicplasty; OCA, osteochondral allograft transplantation; OR, odds ratio; PRISMA, preferred reporting items for systematic reviews and meta-analysis, RCT, randomised control trial.</td></tr>
</table>

Study 3 Pareek A (2016)

Details

Study type	**Systematic review**
Country	US
Recruitment period	Databases search: January 1995 to June 2015
Study population and number	10 studies (3 RCTs, 7 case series), 610 patients
Age and sex	27±3.6 years, 70% male
Patient selection criteria	Inclusion criteria: - English language - Study of any level of evidence reporting knee cartilage repair with minimum of 9 years of follow-up
Technique	Of the included studies, 3 contained cohorts of patients comparing OATM with another cartilage repair procedure. All studies reported mosaicplasty as the procedure of choice, except 1 that used single-plug transfer.
Follow-up	**Mean 10 (9 to 18) years**
Conflict of interest/source of funding	Authors reported having received support from Arthrex, Stryker, VOT solutions, Bioomet, Arthritis Foundation, and Histogenics

Analysis

Follow-up issues: Studies with a minimum of 9-year follow-up were selected.

Study design issues: Modified Coleman methodology score was used to assess study quality. Two authors have independently searched the literature. The literature search was systematic and comprehensive following a PRISMA guideline. Studies reported on activity based outcomes (Tegner activity scale) and clinical outcomes (Lysholm and IKDC scores).
A multiple regression using standard least-squares analysis was constructed to analyse the relation of failure rate with dependent variables such as age, preoperative duration of symptoms, proportion of patients with previous surgery, defect size and proportion of patients with concomitant surgery.

Study population issues:

Study	Study design	Comparators	n in OATM group, follow-up	Defect size (range) cm^2
Bentley 2012	RCT	OATM, ACI	41, 10 years	4 (1 to 2)
Gudas 2012	RCT	OATM, MF	29, 10 years	NR (NR)
Ulstein 2014	RCT	OATM, MF	14, 10 years	3 (2 to 6)
Cognault 2015	Case series	OATM	25, 9 years	2.1 (0.9 to 3)
Filardo 2014	Case series	Single plug (OATM)	15, 18 years	NR (1.5 to 4.5)
Filardo 2015	Case series	OATM	26, 12 years	1.9 (NR)
Hangody 2010	Case series	OATM	303, 10 years	2.5 (1 to 5)
Panics 2012	Case series	OATM	61, 10 years	2.4 (1 to 5)
Solheim 2013	Case series	OATM	73, 12 years	3 (1 to 5)
Tetta 2010	Case series	OATM	24, 9 years	1.9 (1 to 2.5)

Included studies MCMS score was 57.7 ± 11.1 (range 44 to 76, fair). Average body mass index was 24.11±2.2 Kg/m^2. The mean defect size was 2.6±0.5 (range 0.9 to 20) cm^2. The mean duration of symptoms before surgery was 4.8±2 (range 1.8 to 7.6) years.

Eighty-six percent of all lesions were present on the femoral condyles (63% medial femoral condyle, 23% lateral femoral condyle) followed by 7% on the patella, 45 on the trochlea and 3% on the tibial plateau. The mean proportion of patients having previous surgery on the same joint was 55%. There were 48% of patients having concomitant procedures including ACL reconstruction (29%), meniscectomy (10%), high tibial or distal femoral osteotomy (6%) and patellar realignment or lateral retinacular release (4%)

Other issues: the studies by Bentley 2012, Gudas 2012 and Ulstein 2014 were also reported by paper 1 in table 2. The study by Hangody 2010 was also reported by paper 4 in table 2.

Key efficacy and safety findings

Efficacy	Safety
n=10 studies, 610 patients Mean time to weight bearing: 4.7 weeks (n=221) Mean time to full activities: 13.7 weeks **Activity related outcomes and return to sport** **Tegner scores** (0 = lowest level of function, 10 = better level of function) **(5 studies, n=119)** Mean differences from preoperative and postoperative Tegner scores were not statistically significantly different across studies (0.76 [95% CI -0.83 to 2.36], p=0.35) **Rates of return to sport (3 studies, n=114)** Mean return to sport rate across studies was 85% (97/114) **Clinical and functional outcomes** **IKDC score** (0 = lowest level of function, 100 = better level of function) **(3 studies, n=70)** Mean improvement from preoperative to final value was 42.4% (95% CI 31.8 to 53.1, p<0.001) **Lysholm score** (0 = lowest level of function, 100 = better level of function) **(3 studies, n=104)** Mean improvement from preoperative to final value was 21.1 (95% CI 12.2 to 30, p<0.01) **Reoperations and failures** Mean OATM failure rate: 28% (all studies) Mean reoperation rate: 19% (all studies). There were a total of 112 operations reported in 7 of the 10 studies. Of all reoperations 54% were surgical debridement due to symptoms in the same joint, 28% revision cartilage surgery, 14% knee arthroplasty, 3% high tibial or distal femoral osteotomy and 2% surgery unrelated to original cartilage defect. **Risk factor analysis** Failure rate Age at the time of OATM was positively correlated with failure rate (r=0.775, p<0.01), previous surgery (r=-0.689, p<0.01) and defect size (r=0.952, p<0.01) Failure rate correlated negatively with concomitant surgical procedures (r=-0.663, p<0.01) Reoperation rate Reoperation rate was positively correlated to age at time of OATM (r=0.896, p<0.01) and defect size (r=0.863, p<0.01) Reoperation rate was negatively correlated with concomitant surgical procedures (r=-0.790, p<0.01)	Deep infection – less than 1% (2/303) Venous thrombosis – 1% (3/303) **Donor site morbidity** Donor plugs ranged from 3.5 to 8.5mm in diameter. Filardo 2015 (n=26): correlation between the number of plugs and IKDC score[1] (p<0.05) with mean IKDC scores 85 for patients with 1 plug and mean score of 50 for patients with 4 plugs. Patients with 3 or more donor plugs had worse postoperative Kellgren-Lawrence score at follow-up compared with those with 1 or 2 plugs (p=0.044) Tetta 2010 (n=24): Number of plugs did not affect the knee function (ICRS score) or failure rate (p=0.42) and 10-year follow-up. [1]IKDC score (0 = lowest level of function, 100 = better level of function) [2]Kellgren-Lawrence score (0 = no radiological evidence of osteoarthritis to 4 = Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony deformity)
Abbreviations used: ACI, autologous chondrocyte implantation; ACL, anterior cruciate ligament; CI, confidence interval; IKDC, International Knee Documentation Committee score; MF, microfracture; MCMS, modified Coleman methodology score; NR, not reported; OATM, osteochondral autograft transfer mosaicplasty; PRISMA, preferred reporting items for systematic reviews and meta-analysis, RCT, randomised control trial.	

Study 4 Andrade R (2016)

Details

Study type	**Systematic review**
Country	Portugal
Recruitment period	Search date: October 2016
Study population and number	21 studies, 1,726 patients Knee: 11 studies cartilage repair, n=1,472 patients (1,473 injuries) Ankle 10 ankle cartilage repair, n=254 (268 injuries)
Age and sex	Knee – mean 33.2 years Ankle – mean 34.8 years
Patient selection criteria	Inclusion criteria: - Original studies assessing the occurrence of donor site morbidity after mosaicplasty - Follow-up ≥ 6 months - Studies level I to IV - Prospective or retrospective studies with sample size ≥ 10 patients - Human subjects - English language studies Exclusion criteria: - Reviews or meta-analysis - Clinical commentaries, expert opinions or technical notes - Skeletally immature population - Synthetic grafts - Allografts - Mosaicplasty done as complementary procedure for other surgical procedures (such as anterior cruciate ligament transplantation or meniscal transplant) - Cohorts using adhesive patches on the donor site
Technique	Studies were select if they reported on donor site morbidity after mosaicplasty.
Follow-up	**12 to 115 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues:

Study design issues: Two investigators has sifted the literature independently. Study quality assessment used a Coleman methodology score (0 lowest quality to 100 highest quality).

Study population issues:

Author	Study design	n, follow-up
Atik 2005	Case series	12, 48 months
Clave 2000	RCT	25, 24 months
Espregueira-Mendes 2012	Case series	31, 110 months
Gudas 2005	RCT	28, 37 months
Hangody 2008	Retrospective case series	967, more than 12 months
Hangody 2010	Retrospective case series	303, 115 months
Jakob 2002	Case series	42, 37 months
Kock 2010	Case series	13, 49 months
Koulalis 2004	Case series	18, 27 months
Quarch 2014	Case series	16, 14 months
Reverte-Vinaixa 2013	Case series	17, 12 months

Other issues: The systematic review included studies of patients treated by OATM in the knee and ankle. Only efficacy and safety outcomes related to knees treated by OATM were reported. The study by Hangody 2010 was also reported by paper 3 in table 2. The study by Gudas 2005 was also reported in paper 1 and 2 in table 2.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td></td><td>
<table>
<tr><th>Study</th><th>Donor site morbidity</th><th>Frequency</th></tr>
<tr><td>Atik 2005</td><td>None</td><td>-</td></tr>
<tr><td>Clave 2000</td><td>Persistent patellofemoral pain</td><td>4% (1/25)</td></tr>
<tr><td>Espregueira-Mendes 2012</td><td>None</td><td>-</td></tr>
<tr><td>Gudas 2005 RCT</td><td>None</td><td>-</td></tr>
<tr><td>Hangody 2008</td><td>Moderate and severe donor site disturbances</td><td>3% (29/967)</td></tr>
<tr><td>Hangody 2010</td><td>Patellofemoral complaints</td><td>5% (15/303)</td></tr>
<tr><td rowspan="2">Jakob 2002</td><td>Minor postoperative effusion</td><td>1/42</td></tr>
<tr><td>Crepitation</td><td>36% (15/42)</td></tr>
<tr><td>Kock 2010</td><td>Retropatellar crepitus</td><td>92% (12/13)</td></tr>
<tr><td>Koulalis 2004</td><td>Patellar chondropathy</td><td>22% (4/18)</td></tr>
<tr><td></td><td>Joint effusion</td><td>38% (7/18)</td></tr>
<tr><td>Quarch 2014</td><td>Discomfort on the back of the knee during stair climbing or kneeling</td><td>13% (2/16)</td></tr>
<tr><td>Reverte-Vinaixa 2013</td><td>Osteoarthritis</td><td>1/17</td></tr>
</table>
</td></tr>
<tr><td colspan="2">Abbreviations used: RCT, randomised control trial;</td></tr>
</table>

Study 5 Clavé A (2016)

Details

Study type	**RCT**
Country	France
Recruitment period	2007 to 2012
Study population and number	n=55 (30 Cartipatch, 25 mosaicplasty)
Age and sex	Cartipatch: mean age 29.2±11.9 years; 20 males, 10 females Mosaicplasty: mean age 28.3±8.6 years; 20 males, 5 females
Patient selection criteria	Inclusion criteria: - Age 18 to 50 - Solitary femoral-condyle chondral defect grade III and IV (ICRS classification) - Defect size 2.5 to 7.5 cm^2 (assessed using the rectangle technique, 2.5 cm^2 corresponds to a diameter of 1.58 cm and 7.5 cm^2 to a diameter of 2.75 cm^2) - Incapacitating symptoms (IKDC score <55) Exclusion criteria: - Pregnancy or breastfeeding - History of anaphylaxis to gentamicin or amphotericin B - Kissing lesion of the patella or tibia - Patellar abnormality - Osteoarthritis grade >2 - Varus or valgus>10° - Uncorrected ligamentous or meniscal lesion - Total menisectomy - Anteroposterior laxity (Lachmann>3) - History of cancer or autoimmune disease - Systemic bone, joint or muscular disease - History of chronic use of medication known to affect bone metabolism - Positive test for HIV, hepatitis B or hepatitis C - Body mass index>30 kg/m^2 - Multiple food allergies (particularly seafood) - Surgical procedure done on the same knee less than 18 months before
Technique	Patients were randomised to third generation ACI using an agarose-alginate scaffold (Cartipatch) or mosaicplasty in patients with isolated symptomatic femoral chondral defects (ICRS III and IV). Histological evaluation based on the O'Driscoll score was done at 2 years (range 0 to 21). All procedures were done by experienced surgeons and no concomitant procedures were done. Single stage mosaicplasty was done with or without tourniquet. The number and size of the plugs varied with the size of the defect. A brace and crutches were used postoperatively for 30 days and mobilisations between 0 and 90° were allowed, but weight bearing was eliminated. One month after the procedure partial weight bearing with crutches and a wider range of joint motion were allowed. At 2.5-month full weight bearing without support and full range of articular motion were allowed.
Follow-up	**2 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Data were collected by blind observers preoperatively then 3, 6, 12 and 24 months postoperatively. At 2 years, 6 patients were lost to follow-up in the Cartipatch group and 2 in the mosaicplasty group.

Study design issues: An independent institution generated an automatic 1:1 permutated block randomisation. Seventy-six patients were needed to demonstrate an at least 10-point subjective IKDC score difference with α=5% and 90% power. The primary outcome was to summarise the IKDC score 2 years after surgery.

All patients had the randomly allocated treatment. The data were analysed by an independent statistician.

Defect size (cm^2)

Group	Preoperative (MRI)	Intraoperative before debridement	Intraoperative after debridement
Mosaicplasty	3.6±1.8	3.5±0.3	4.07±0.8
Cartipatch	3.2±1.3	3.1±0.8	3.9±0.8

Study population issues: Treated lesions were 2.5 to 7.5 cm^2 in diameter. The baseline characteristics of the 2 groups were not significantly different.

Other issues: None

Key efficacy and safety findings

Efficacy

n=55 (30 Cartipatch, 25 mosaicplasty)

Mean IKDC score

Mean IKDC score, mean±SD	n	Preoperative Mean±SD	24-month Mean±SD	Improvement Mean±SD
Mosaicplasty	23	37.2±12	81.5±16.4	44.3±15.2
Defect ≤3.5 cm^2	9	35.4±12.1	76±13.4	40.6±16.7
Defect >3.5cm^2	14	39.5±11.6	85.1±17.1	45.6±13.6
Cartipatch	24	41.9±8.9	73.7±20.1	31.8±20.8
Defect ≤3.5 cm^2	14	40.9±9.2	78.9±17.4	38±15.8
Defect >3.5cm^2	10	41.9±8.8	68.4±22.1	25.4±24.3
Mean difference	**-**	**-4.7, p=0.43**	**-**	**12.6, p=0.028**

The IKCD score was not influenced by BMI (p=0.83), time from onset to index surgery (p=0.61), mode of symptom onset (p=0.79), cause of injury (p=0.45), sports level (p=0.79), limb alignment (p=0.09), surgical knee history (p=0.67) and number and size of the plugs used (p=0.52)

Histology

n=47 patients, 47 samples

Mean O'Driscoll score (range 0 to 21, higher score meaning better cartilage repair) was 15.1±3.7 (range 10 to 19) in the Cartipatch group and 18.5±2.5 (range 14 to 21) in the mosaicplasty group, meaning a significant 3.3-point difference (p=0.02).

The O'Driscoll score was not statistically significantly different between groups with defects <3.5cm^2 (p=0.43) or ≥3.5 cm^2 (p=0.28).

Safety

	Cartipatch Events (patients)	Mosaicplasty Events (patients)	p
Intra-articular effusion	7 (6)	4 (2)	0.19
Haematoma	2 (2)	1	0.53
Popliteal cyst	1	1	0.75
Persistent patella-femoral pain	0	1	0.5
Complex regional pain syndrome	1	0	0.51
Post-operative joint infection	1*	0	0.51
Total	**12 (10)**	**6 (4)**	**0.08**

*The investigation of this event found no evidence of cell sample contamination.

Abbreviations used: ACI, autologous chondrocyte implantation; BMI, body mass index; ICRS, International Cartilage Repair Society; IKDC, International Knee Documentation Committee; MRI, magnetic resonance imaging; RCT, randomised control trial; SD, standard deviation.

Study 6 Ollat D (2011)

Details

Study type	**Retrospective case series**
Country	France
Recruitment period	Not reported
Study population and number	**n=142 (61 osteochondritis dissecans, 79 osteochondral fractures)** defects of the knee
Age and sex	Osteochondritis dissecans: mean age 26±9, 74% (45/61) males Osteochondral fractures: mean age 34.3±12, 78% (62/79) males
Patient selection criteria	Inclusion criteria: - Osteochondral defects regardless of aetiology - Age between 16 and 50 years - At least 5 years of follow-up Exclusion criteria: - Osteonecrosis in elderly patients and osteochondritis in patients over 50 were excluded
Technique	Patients were recruited from 13 reference centres. Evaluation of the initial defect size was based on the surgical report defect depth was based on the ICRS score. Open surgery was done in 114 cases and by arthroscopy in 28 cases. There were three technical variants: pin plug fixation (n=15), interplug filling (n=9), fixation plus (n=4) internal fixation with a screw, and plug mosaicplasty according to Beaufils. Postoperatively 52% of patients were immobilised. Full weight bearing was possible after a mean of 7 weeks.
Follow-up	**Mean 96±28 (range 53 to 158) months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: None.

Study design issues: Retrospective study.

Study population issues: Mean BMI was 25 (range 21 to 41). Fifth-three percent of knees had a history of surgery. Mean delay between the accident and surgery was 2.5 years. Mean are of defect was 2.29 cm^2 (range 0.3 to 12.25 cm^2). Depth of the defect was 3 or 4 on the ICRS score in 97% of the cases. An additional procedure was associated with mosaicplasty in 14% of the cases. Most defects were located in the internal condyle (75% medial condyle, 17% lateral condyle, 5% patella, 3% trochlea). The number of transplanted plugs was 4 (range 1 to 14) and the mean diameter of the plug was 4. 5mm (n=58).

Outcomes of interest at follow-up were level of sports activity, Hughston score, ICRS score and IKDC subjective score. Morphological analysis at the final follow-up used a Brittberg classification when there was a second look by arthroscopy or by CT arthrography and follow-up MRI when they could be interpreted. Mean sick leave was 13 weeks.

Other issues: None

Key efficacy and safety findings

Efficacy	Safety
n=142 (61 osteochondritis dissecans, 79 osteochondral fractures) **Functional results** Most patients (82%) were very satisfied or satisfied. At follow-up there was significant clinical improvement in ICRS scores (p<0.001), IKDC function (p<0.001) and Hughston scores[1] (p<0.001). The greater the delay from accident to surgery, the worse the IKDC score (p=0.03). The greater the delay between the surgery and follow-up, the lower the IKDC score (p<0.001). Osteochondritis patients had more often a Hughston score of 4 than patients in the chondral fracture group (p=0.001). Males had in average a better objective IKDC score (p=0.009). Patients with lesion depth of IV in the ICRS score had better outcome than patients with depth scores of II and III (p value not reported). Patients with medial condyle defects had better ICRS clinical and Hughston scores than patients with lateral condyle or patellofemoral compartment defects (p=0.009). Patients with defects smaller than 2 cm^2 had Hughston scores of 3 or 4 more frequently than patients with defects between 2 and 4 cm^2 (p=0.05). There were 35 arthroscopies done at follow-up, in 31% (11/35) graft integration was considered complete. At follow-up 80% of patients had Hughston radiological score of 3 or 4. Patellofemoral osteoarthritis was present in 13% of cases. A modified11-point MOCART (higher score meaning better cartilage repair) score was created based on MRI examinations and mean score was 7 (range 4 to 10). [1]Hughston score (0=restriction of sports, to 4=normal sport activities)	<u>Complication rate:</u> 13% (19/142)[2] <u>Haemarthosis</u>: 4% (6/142) <u>Sepsis</u>:1/142 <u>Complex regional pain syndrome</u>: 1/142 <u>Patellofemoral osteoarthritis (stage C or D on the IKDC score</u>): 13% of cases. [2]No specification made in regards to the remaining 11 patients having complications.
Abbreviations used: BMI, body mass index; CT, computerised tomography; ICRS, International Cartilage Repair Society; IKDC, International Knee Documentation Committee; MOCART, magnetic resonance observation of cartilage repair tissue; MRI, magnetic resonance imaging; SD, standard deviation.	

Study 7 Kosiur JR (2014)

Details

Study type	**Retrospective case series**
Country	US
Recruitment period	1997 to 2012 **Group A**: September 1998 to May 2001 **Group B**: December 2001 to September 2011 **Group C**: November 2001 to September 2011
Study population and number	**n=534**, patients treated by OAT **Group A**: 68 OAT procedures, 67 patients **Group B**: 29 OAT procedures with concomitant ACL reconstruction, 29 patients **Group C**: 437 OAT procedures, 425 knees, 402 patients 23 patients had bilateral OAT and 20 patients (7 from group A and 1 from group B and 12 from group C) had repeat OAT
Age and sex	**Group A**: 47.7±7.34 years, 43% (29/67) males **Group B**: 39.1±10.65 years, 52% (15/29) males **Group C**: 51±10.93 years, 38% (152/402) males
Patient selection criteria	Consecutive patients treated by OAT between 1997 and 2012.
Technique	Chart review of consecutive 567 arthroscopies (544 knees, 512 patients), arthroscopic OAT of symptomatic cartilage defects that were grade III or IV according to the Outerbridge classification system. All patients treated by OAT before June 2001 were kept non-weight bearing for 4 weeks postoperatively. After June 2011, 1 of the 3 protocols were followed: non-weight bearing, 50% weight bearing or full weight bearing. Three groups were formed accordingly: - Group A: non-weight bearing for 4 weeks and full weight bearing thereafter - Group B: non-weight bearing for 4 weeks and full weight bearing thereafter - Group C: weight bearing as tolerated No patient had deep vein thrombosis prophylaxis. Patients were advised not to engage in high impact activities for 3 months after the procedure. A range of motion exercises were started immediately after surgery. From July 2000 to May 2012, 62 consecutive knees (59 patients) had repeated arthroscopy. From these, 11 group A patients and 9 group B patients were pooled into a sub-group (non-weight bearing), n=20. Second look patients from group C were stratified into a second group (weight bearing as tolerated), n=42. Repeated OAT were done in selected cases for Outerbridge grade III and IV defects that developed adjacent to the OAT original repair.
Follow-up	**Non-weight bearing:** 39.4±33.1 months (range 2.5 to 132) **Weight bearing as tolerated:** 32.7±24.9 months (range 1 to 113)
Conflict of interest/source of funding	None.

Analysis

Follow-up issues: There was no significant difference in the duration of follow-up between the subgroups for repair-adjacent defects and graft position or macroscopic assessment of the outcome.

Study design issues: The study main author carried out all the procedures. Patients treated between mid-June and October 2001 were eliminated from the analysis so that selection bias could be eliminated and homogeneous groups of consecutive patients could be established.

Primary outcomes were assessed according to resolution of pain with weight bearing activities, postoperative complications and repeat OAT rates across the 3 groups. Secondary outcomes included repair-adjacent defect prevalence, graft position, and macroscopic assessment of the of cartilage repair in the second look.

Study population issues: Graft diameter ranged from 4.5 to 11 mm and all grafts were 15 mm in length.

A total of 69 OAT repaired defects and 93 grafts were examined in the 2 second look groups. However, the chondral margins for the grafts of 12 OAT repaired defects in 11 knees (3 non-weight bearing and 9 weight bearing as tolerated) could not be identified or delineated from the articular surface or native cartilage during second arthroscopic examination. Images were not made and were not available for review.

Three further pictures were not able to be used in the macroscopic cartilage assessment: 1 photograph was blurry, 1 graft used in the repair was mal-united and 1 repair was only partially photographed.

One graft used to repair 1 of the 2 defects in 1 knee was damaged by traumatic knee injury and was excluded from all 3 outcome assessments.

- A total of 53 OAT repaired defects (17 non-weight bearing, 36 weight bearing as tolerated) were included in the blinded macroscopic assessment of cartilage repair.
- A total of 92 of 93 grafts (30 non-weight bearing, 62 weight bearing as tolerated) had documented valuations of graft position.
- A total of 68 of 69 OAT repaired defects (22 non-weight bearing, 46 weight bearing as tolerated) had documented valuations of repair-adjacent defects.
- All 233 patients with documented valuations for pain with weight bearing activities both preoperatively and postoperatively were included.

Other issues: None.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>

n=534 OAT procedures

Graft position, repair-adjacent defects and ICRS score

Graft position: no statistically significantly difference between groups (n=91), p=0.99

Good joint congruity maintained in 95% (21/22) non-weight bearing and 100% (46/46) weight bearing as tolerated subgroups.

There was no difference in the frequency of repair of adjacent defects between non-weight bearing and weigh bearing as tolerated groups, p=0.94.

The mean total ICRS macroscopic cartilage repair score was 0.13 points higher (95% CI -0.605 to 0.345) in the weight bearing as tolerated group, p=0.71.

Resolution of pain

There was no difference in pain resolution between group A (non-weight bearing) and C (weight bearing as tolerated), p=0.25.

Repeated surgeries

The weight bearing as tolerated group experienced significantly fewer repeated OAT compared with the non-weight bearing group, p<0.001.

Concomitant surgery

Non-weight bearing with concomitant ACL reconstruction (group B) had no significant effect on secondary outcomes compared with non-weight bearing without concomitant ACL (group A).

</td><td>

The weight bearing as tolerated group experienced significantly fewer DVT and arthrofibrosis compared with the non-weight bearing group, p<0.001.

Complication	Group A (OAT)	Group B (OAT+ACL)	p	Group C (weight bearing)	p
n	68	29	-	437	-
DVT	3% (2/68)	3% (1/29)	0.28	1% (3/437)	<0.001
Pulmonary embolism	2% (1/68)	0	<0.001	0	<0.001
Arthrofibrosis	5% (3/68)	7% (2/29)	0.01	0	<0.001
Haemarthrosis	0	0	-	Less than 1% (1/437)	<0.001
Infection	0	0	-	Less than 1% (2/437)	<0.001

</td></tr>
<tr><td colspan="2">Abbreviations used: ACL, anterior cruciate ligament; DVT, deep vein thrombosis; ICRS score, ICRS, International Cartilage Repair Society; OAT, osteochondral autograft transfer</td></tr>
</table>

Study 8 Krytch AJ (2012)

Details

Study type	**Non-randomised control study**
Country	US
Recruitment period	1999 to 2009
Study population and number	**n=96 (48 OAT, 48 MF),** patients with full cartilage defects of the femoral condyles or trochlea
Age and sex	OAT: mean 29.7 years, 67% (32/48) males MF: mean 32.5 years, 67% (32/48) males
Patient selection criteria	Inclusion criteria: - Skeletal maturity - Single symptomatic cartilage lesion of the medial condyle, lateral condyle or trochlea of the femur that was classified as Outerbridge grade III or IV at the time of initial arthroscopy and did not involve substantial bone loss - Lesion area of 1 to 6 cm^2 - Minimum of 2 years of follow-up - Age between 15 and 50 years Exclusion criteria: - Generalised osteoarthritis, osteonecrosis, lower extremity malalignment, ligamentous instability or concomitant stabilisation procedures involving more than 1 ligament, inflammatory arthritis,
Technique	The institutional registry was used to match each patient in the OAT group with a patient in the MF group. A diagnostic arthroscopy was done in every patient to assess additional intraarticular abnormalities. Donor osteochondral plugs were harvested by hand using a commercially available instrument (Arthrex, Florida). Patients in both groups had the same postoperative rehabilitation. For patients with a lesion of the medial lateral femoral condyle, continuous passive motion from 0 to 60° was started in the recovery room and the range was increased until full passive motion was achieved. This was continued for 6 hours a day for 6 weeks, after which weight bear was permitted. Patients with trochlear lesions were permitted to bear weight as tolerated with the knee in full extension, flexion was limited to 0 to 20°. Passive motion was maintained for 6 hours a day for 6 weeks. Return to normal activities was achieved at 6 to 8 months postoperatively.
Follow-up	**MF: Mean 4.4 years (range 2 to 10)** **OAT: 3.1 years (range 2 to 10)**
Conflict of interest/source of funding	One or more authors have declared receiving payments or services, either directly or indirectly from a third party. One or more authors have declared being involved with a biomedical entity that could be perceived to influence what is written in the report.

Analysis

Follow-up issues: patients were prospected evaluated at baseline and then at 1, 2, 3 and 5 years postoperatively.

Study design issues: Power calculation indicated that 35 patients per group would be needed to show differences in the SF-36, IKDC, KOSADL and MARS instruments between the groups with an effect size of 0.8, α=0.05 and β=95%. Bonferroni adjustments of the p value threshold for significance were done when analysing multiple comparators, from 0.05 to 0.013.

Study population issues: Mean BMI was 25.5 kg/m^2 in the MF group and 25.2 kg/m^2 in the OAT group. Both groups included 27 chondral lesions of the medial femoral condyle, 16 of the lateral femoral condyle and 5 of the trochlea. The mean size of the defect was 2.55 cm^2 (range 1 to 6.25) in the MF group and 2.65 cm^2 (1 to 6.25) in the OAT group.

In the MF group, aetiology of injury was chronic or atraumatic in 23 patients, traumatic in 22 and osteochondritis dissecans in 3. In the OAT group, the aetiology of injury was chronic or atraumatic in 13 patients, traumatic in 20 and osteochondritis dissecans in 15.

In the MF group no patient had previous cartilage surgery, in the OAT group 16 patients had previous been unsuccessfully treated with MF. Concomitant procedures in the MF group included 3 meniscal repairs in the affected

compartment, 3 arthroscopic partial meniscectomies involving the affected compartment and 1 lateral retinacular release. Concomitant procedures in the OAT group included 1 meniscal repair in the affected compartment, 5 arthroscopic partial meniscectomies in the affected compartment and 1 lateral retinacular release.

Baseline characteristic were identical in both matched groups.

The plug diameters ranged 6 to 10 mm and the typical plug depth was 8 to 10 mm. the mean number of plugs transferred was 2.7 (range 1 to 10) with only 2 patients having more than 5 plugs.

Other issues: None

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>n=96 (48 OAT, 48 MF)

<u>Quality of life</u>
SF-36 score improved significantly from baseline assessment to 1, 2, 3 and 5 years postoperatively (p<0.01) but was not statistically significantly different between OATM and MF groups.
<u>Knee function</u>
The KOSADL score and the IKDC score improved statistically significantly from baseline to 1, 2, 3 and 5 years postoperatively in both groups (p<0.01 for all). The scores did not differ significantly between the groups at any point.
Activity level
MARS score (range 0 to 10, higher score indicates more functional demand on the knee joint)
<table>
<tr><th>Follow-up</th><th>Baseline</th><th>1 year</th><th>2 years</th><th>3 Years</th><th>5 Years</th></tr>
<tr><td>OAT</td><td>6.4±6.4</td><td>5.21±2.3, p=0.49</td><td>7.29±1.24, p=0.28</td><td>7.75±2.24, p=0.63</td><td>8.55±2.31, p=0.22</td></tr>
<tr><td>MF</td><td>7.3±5.4</td><td>4.11±1.05, p=0.02</td><td>3.71±1.64, p<0.001</td><td>2.91±2.12, p=0.02</td><td>2.89±2.5, p=0.02</td></tr>
</table>
MARS was statistically significantly better in the OAT group when compared with the MF group at 2 (p=0.001), 3 (p=0.03) and 5 (p=0.02) years postoperatively.</td><td>None reported.</td></tr>
<tr><td colspan="2">Abbreviations used: BMI, body mass index; IKDC, International Knee Documentation Committee score; KOSADL, Knee Outcome Survey Activities of Daily Living; MARS, Marx Activity Rating Scale; MF, microfracture; OAT, osteochondral autograft transfer; SF-36, Short Form 36.</td></tr>
</table>

Validity and generalisability of the studies

- There is extensive available evidence including randomised studies with medium to long-term follow-up data (10 years)[1-4, 7].
- Most of the evidence is from outside the UK but 1 large RCT by Bentley is included in the overview[1-3].
- There is some overlap between the systematic reviews and meta-analysis included in table 2[1-4].
- The evidence was based on different devices but this was frequently not reported in the studies.

Existing assessments of this procedure

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

Related NICE guidance

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

Interventional procedures

- Microstructural scaffold (patch) insertion without autologous cell implantation for repairing symptomatic chondral knee defects. Interventional procedures guidance 560 (2016). Available from https://www.nice.org.uk/guidance/ipg560

Technology appraisals

- The use of autologous chondrocyte implantation for the treatment of cartilage defects in the knee joints. NICE Technology appraisal guidance 89 (2005). Available from https://www.nice.org.uk/guidance/ta89

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Specialist Advisor Questionnaires for mosaicplasty for symptomatic articular cartilage defects of the knee were submitted and can be found on the NICE website.

Patient commentators' opinions

Section to be inserted if there is patient commentary

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

Section to be inserted if there is no patient commentary at IPAC 1

NICE's Public Involvement Programme will send questionnaires to 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.

Section to be inserted if there is no patient commentary at IPAC 2

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

Section to be inserted if patient commentators raised no new issues

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers. [Add if relevant: See the patient commentary summary for more information.]

Section to be inserted if patient commentators raised new issues

The patient commentators raised the following issues about the safety/efficacy of the procedure, which did not feature in the published evidence or the opinions of specialist advisers, and which the committee considered to be particularly relevant:

- [insert additional efficacy and safety issues raised by patient commentators and highlighted by IPAC, add extra rows as necessary].
- [Last item in list].

[Add if relevant: See the patient commentary summary for more information.]

Company engagement

A structured information request was sent to 3 companies who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. These 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 terms mosaicplasty and osteochondral autograft transfer refer to slight variations of the same procedure and may have been used interchangeably in the literature.
- No emerging key trial was found.

References

1. Lynch TS, Patel RM, Benedick A et al. (2015) Systematic review of autogenous osteochondral transplant outcomes. Arthroscopy: the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 31: 746-54
2. Riboh JC, Cvetanovich GL, Cole BJ et al. (2016) Comparative efficacy of cartilage repair procedures in the knee: a network meta-analysis. Knee Surg Sports Traumatol Arthrosc (online)
3. Pareek A, Reardon PJ, Maak TG et al. (2016) Long-term outcomes after osteochondral autograft transfer: a systematic review at mean follow-up of 10.2 years. Arthroscopy - Journal of Arthroscopic and Related Surgery 32: 1174-1184
4. Andrade R, Vasta S, Pereira R et al.(2016) Knee donor-site morbidity after mosaicplasty - a systematic review. Journal of experimental orthopaedics 3: 31
5. Clave A, Potel JF, Servien E et al. (2016) Third-generation autologous chondrocyte implantation versus mosaicplasty for knee cartilage injury: 2-year randomized trial. Journal of orthopaedic research : official publication of the Orthopaedic Research Society 34: 658-65
6. Ollat D, Lebel B, Thaunat M et al. (2011) Mosaic osteochondral transplantations in the knee joint, midterm results of the SFA multicenter study. Orthopaedics & traumatology, and surgery & research : OTSR 97: S160-6
7. Kosiur JR and Collins RA (2014) Weight-bearing compared with non-weight-bearing following osteochondral autograft transfer for small defects in weight-bearing areas in the femoral articular cartilage of the knee. The Journal of bone and joint surgery. American volume 96: e136
8. Krych AJ, Harnly HW, Rodeo SA et al. (2012) Activity levels are higher after osteochondral autograft transfer mosaicplasty than after microfracture for articular cartilage defects of the knee: a retrospective comparative study. The Journal of bone and joint surgery. American volume 94: 971-8

Additional relevant papers

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
Andrade R, Vasta S, Papalia R et al. (2016) Prevalence of Articular Cartilage Lesions and Surgical Clinical Outcomes in Football (Soccer) Players' Knees: A Systematic Review. Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 32: 1466-77	Systematic review n=5 studies FU=minimum 12 months	No definitive conclusion could be made in respect to the best current surgical technique for articular cartilage and osteochondral lesions. Microfracture and mosaicplasty can provide a faster return to competition and faster clinical and functional results, whereas autologous chondrocyte implantation or matrix-induced autologous chondrocytes implantation procedures can enhance longstanding clinical and functional results.	Reports on time to sport only. No new safety data.
Astur DC, Arliani GG, Binz M et al. (2014) Autologous osteochondral transplantation for treating patellar chondral injuries: evaluation, treatment, and outcomes of a two-year follow-up study. The Journal of bone and joint surgery. American volume 96: 816-23	Case series n=20 FU=2 years	Autologous osteochondral transplantation is a successful technique to surgically treat symptomatic full-thickness patellar articular cartilage injuries smaller than 2.5 cm in diameter. Patients had a significant improvement in clinical scores. Bone-plug integration and surface alignment were seen in all patients 2 years after surgery.	Larger case series already included. No new safety events.
Astur DC, Bernardes A, Castro S et al. (2016) Functional outcomes after patellar autologous osteochondral transplantation. Knee Surgery Sports Traumatology Arthroscopy	Case series n=33 FU=2 years	Autologous osteochondral transplantation for the treatment of patellar chondral lesion was associated with significant improvement in pain, gait, swelling, and range of motion 2 years after surgery, achieving scores similar to uninjured knees. Most of them were able to return to sports activity after 6 months (recreational level) and 2 years (competitive level).	Larger case series already included. No new safety events.
Atik OS, Uslu MM and Eksioglu F (2005) Osteochondral multiple autograft transfer (OMAT) for the treatment of cartilage defects in the knee joint. Bulletin (Hospital for Joint Diseases (New York, and N.Y.)) 63: 37-40	Case series n=12 FU=4 years	Second-look arthroscopy (5 patients) demonstrated a normal shiny appearance and colour of the grafted area. We saw slight joint effusion postoperatively that disappeared in 2 months. There was no donor site morbidity. OMAT is a promising surgical technique for the treatment of articular cartilage defects. Long-term follow-up with more patients and histological and biomechanical evaluation of chondral interfaces are the subjects of our continuing study.	Reported in paper 4 in table 2.

Baltzer AWA, Ostapczuk MS, Terheiden HP et al. (2016) Good short- to medium-term results after osteochondral autograft transplantation (OAT) in middle-aged patients with focal, non-traumatic osteochondral lesions of the knee. Orthopaedics & traumatology, and surgery & research 102: 879-884	Case series n=112 FU=26 months	Pain (pre-OAT VAS vs. post-OAT VAS: 7.14±0.19 vs. 3.74±0.26, P<0.001) was reduced and quality of life (pre-OAT WOMAC vs. post-OAT WOMAC: 134.88±5.84 vs. 65.92±5.34, P<0.001) improved. Retropatellar defects were associated with poor outcome, while overall surface and number of cylinders were not.	Larger case series included. No new safety events.
Barber FA and Chow JCY (2006) Arthroscopic chondral osseous autograft transplantation (COR procedure) for femoral defects. Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 22: 10-6	Case series n=36 FU=48 months	This technique successfully transplants chondral osseous grafts within the knee that remain viable. No radiographic arthritic changes were seen and the midterm clinical result was favourable for these patients. Further investigation of the long-term results is needed.	Larger case series included. Large percentage of loss to follow-up.
Bekkers Joris E. J, Inklaar Melanie, and Saris Daniel B. F (2009) Treatment selection in articular cartilage lesions of the knee: a systematic review. The American journal of sports medicine 37 Suppl 1, 148S-55S	Systematic review n=4 RCTs FU=6 to 60 months	Lesion size, activity level, and patient age are factors that should be considered in selecting treatment of articular cartilage lesions of the knee. In addition, these factors are a step toward evidence-based, instead of surgeon-preferred, treatment of articular cartilage lesions of the knee.	Relevant papers already included in table 2. No new safety events.
Bentley G, Biant L C, Vijayan S, Macmull S, Skinner J A, and Carrington R W. J (2012) Minimum ten-year results of a prospective randomised study of autologous chondrocyte implantation versus mosaicplasty for symptomatic articular cartilage lesions of the knee. The Journal of bone and joint surgery. British volume 94: 504-9	RCT n=100 FU=10 years	The number of patients whose repair had failed at ten years was ten of 58 (17%) in the ACI group and 23 of 42 (55%) in the mosaicplasty group ($p < 0.001$). The functional outcome of those patients with a surviving graft was significantly better in patients who had ACI compared with mosaicplasty ($p = 0.02$).	Already reported in other papers in table 2.
Braun S, Minzlaff P, Hollweck R et al. (2008) The 5.5-year results of MegaOATS--autologous transfer of the posterior femoral condyle: a case-series study. Arthritis research & therapy 10(3), R68	Case series n=36 FU=5.5 years	Patients significantly improve in the Lysholm score, in daily-life activity levels and in return to recreational sports. Thirty-one out of 33 patients were comfortable with the results and would have the procedure again. The Mega OATS technique is therefore recommended as a salvage procedure for young individuals with large osteochondral defects in the weight-bearing zone of the femoral condyle.	Larger case series already included.
Carulli C, Matassi F, Soderi S et al. (2014) Open traumatic osteochondral fracture of the femoral medial condyle and trochlea treated by mosaicplasty: a case report at 11-year follow-up. HSS journal : the musculoskeletal journal of	Case report n=1 FU=11 years	A mosaicplasty procedure was successfully done in an open comminuted fracture of the knee, showing long-lasting clinical outcomes. The outcomes were correlated with the young age of the patient.	Larger case series already included. No new safety events.

Hospital for Special Surgery 10: 276-9			
Chadli L, Cottalorda J, Delpont M et al. (2017) Autologous osteochondral mosaicplasty in osteochondritis dissecans of the patella in adolescents. International orthopaedics 41: 197-202	Case series n=8 FU=29 months	Autologous osteochondral mosaicplasty seems to be a reliable technique to manage osteochondritis dissecans of the patella in adolescents on the short term to restore patellar joint surface and obtain satisfactory functional results.	Larger case series already included. No new safety events.
Cognault J, Seurat O, Chaussard C et al. (2015) Return to sports after autogenous osteochondral mosaicplasty of the femoral condyles: 25 cases at a mean follow-up of 9 years. Orthopaedics & traumatology, and surgery & research 101: 313-7	Case series n=9 FU= 9 years	The radiologic evaluation of 21 patients showed complete osteointegration of the grafts in 90% of cases. The results of the femoral condyle mosaic autografts are satisfactory, a mean of 9 years after surgery. The most active patients lowered their activity level while the more sedentary did not have to adapt their lifestyle.	Larger case series already included. No new safety events.
De Almeida LN, Ozorio, Da Silveira F et al. (2010) Surgical treatment of osteochondral lesions of the knee by means of mosaicplasty. Revista brasileira de ortopedia 45. 166-73	Case series n=27 FU=2.5 years	Mosaicplasty proved to be a good alternative for treating osteochondral lesions of the knee. It presented better evolution in relation to lesions of the femoral condyles than in relation to lesions located on the patella.	Larger case series already included. No new safety events.
Dere JJ, Yacuzzi CH and Paz MC (2014) Autologous osteochondral transfer for the treatment of full-thickness defects in patients with or without ACL reconstruction. Results with 7 years follow-up. Orthopaedic Journal of Sports Medicine 2	Case series n=25 FU=5	The results of the mosaicplasty for the focal full-thickness chondral lesions in the femoral condyles are favourable after 5 years of follow up. There was no difference between the associated or not ACL injury.	Larger case series already included. No new safety events.
DiBartola AC, Everhart JS, Magnussen RA et al. (2016) Correlation between histological outcome and surgical cartilage repair technique in the knee: A meta-analysis. The Knee 23: 344-9	Meta-analysis n= 33 studies (7 OATS) FU= up to 10 years	Microfracture has poorer histologic outcomes than other cartilage repair techniques. OATS repairs primarily are comprised of hyaline cartilage, followed closely by cell-based techniques, but no significant difference was found cartilage quality using ICRS grading criteria among OATS, ACI-C, MACI, and ACI-P	Relevant papers already included in table 2. No new safety events.
Dozin B, Malpeli M, Cancedda R et al.(2005) Comparative evaluation of autologous chondrocyte implantation and mosaicplasty: a multicentered randomized clinical trial. Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine 15: 220-6	RCT n=47 FU=36 months	Although the low power of our study prevents definitive conclusions, ACI and mosaicplasty are cartilage repair techniques that are clinically equivalent and similar in performance. The high percentage of spontaneous improvement (1/3 of the patients) seen after simple debridement calls into question the need for prompt surgical treatment of patients with lesions similar to those included in this clinical trial. Moreover, this finding warrants further investigation, ideally through randomised clinical trials in which patients subjected to debridement alone are compared with patients having reconstructive surgery.	The study was underpowered due to high loss to follow-up. No new safety events.
Duif C, Koutah MA, Ackermann O et al. (2015) Combination of	Case report n=1	The simultaneous use of different techniques for cartilage repair may	Larger case series already included.

autologous chondrocyte implantation (ACI) and osteochondral autograft transfer system (OATS) for surgical repair of larger cartilage defects of the knee joint. A review illustrated by a case report. Technology and health care : official journal of the European Society for Engineering and Medicine 23: 531-7	FU=7 months	provide alternative operative solutions for single complex cases, although further studies are needed for a general recommendation.	No new safety events.
Eajazi A, and Sharifzadeh S R (2011) Clinical Assessment of Athroscopic Osteochondral Autograft Transfer (Mosaicplasty) for Cartilage Defects of the Knee. A Prospective Medium-Term Follow-up Study. European Journal of Medical Research 16: 65	Case series n=56 FU=21 months	The findings of our medium-term study indicate that arthroscopic mosaicplasty proves an appropriate option for advanced cartilage lesions of the knee, particularly when it is done for younger patients alongside other disorders of the knee.	Larger case series already included. No new safety events.
Emre TY, Cift H, Seyhan B et al.(2011) Midterm results of biologic fixation or mosaicplasty and drilling in osteochondritis dissecans. Indian journal of orthopaedics 45: 445-9	Case series n=14 FU=2 years	Biologic fixation or mosaicplasty and drilling as a technique to treatment of the lesion in OCD by osteochondral autograft transfer has resulted in good and excellent clinical outcomes in our patients and it is considered that providing blood flow to subchondral bone by circumferential drilling leads to an increase in the robustness of biological internal fixation and shortens the duration of recovery.	Larger case series already included. No new safety events.
Emre TY, Ege T, Kose O et al. (2013) Factors affecting the outcome of osteochondral autografting (mosaicplasty) in articular cartilage defects of the knee joint: retrospective analysis of 152 cases. Archives of orthopaedic and trauma surgery 133: 531-6	Case series n=152 FU=18 months	Mosaicplasty is an effective technique for the treatment of articular cartilage defects of the knee joint which restores the joint function in a short period of follow-up. Furthermore, age, lesion size, localization, and concomitant surgical interventions are major factors affecting the final outcome. The final knee score deteriorates as the age of the patient and size of the lesion increases. Furthermore, concomitant surgical interventions and lesions located on the medial femoral condyle have a negative effect on the final knee score.	Larger case series already included. No new safety events.
Emre TY, Atbasi Z, Demircioglu DT et al. (2016) Autologous osteochondral transplantation (mosaicplasty) in articular cartilage defects of the patellofemoral joint: retrospective analysis of 33 cases. Musculoskeletal Surgery	Case series n=11 FU=1 year	Mosaicplasty is an effective technique for the treatment of articular cartilage defects of the patellofemoral joint knee which restores the joint function in a short period of follow-up. However, a meticulous surgical technique should be followed to restore the native articular surface and the congruity of the joint.	Larger case series already included. No new safety events.
Erdil M, Bilsel K, Taser O et al. (2013) Osteochondral autologous graft transfer system in the knee; mid-term results. The Knee 20: 2-8	Case series n=64 FU= 82 months	All patients showed increasing results in the Lysholm knee scores, Tegner activity scale scores, and IKDC subjective knee evaluation form. Moreover, we found no significant	Larger case series already included. No new safety events.

		correlation between functional results and age, functional results and localization of osteochondral defect, functional results and additional knee pathologies.	
Erol MF and Karakoyun O (2016) A new point of view for mosaicplasty in the treatment of focal cartilage defects of knee joint: honeycomb pattern. SpringerPlus 5: 1170	Case series n=6 FU=6 months	The early outcomes of OAT mosaicplasty with HOGS are comparable to studies on the classical mosaicplasty. According to our observations in this study we can say that the gap space left between the cylindrical plugs can be solved by using hexagonal prism shaped plugs.	Larger case series already included. No new safety events.
Espregueira-Mendes J, Pereira H, Sevivas N et al. (2012) Osteochondral transplantation using autografts from the upper tibio-fibular joint for the treatment of knee cartilage lesions. Knee surgery, sports traumatology, and arthroscopy : official journal of the ESSKA 20:1136-42	Case series n=31 FU=9 years	The level of patient satisfaction was evaluated, and 28 patients declared to be satisfied/very satisfied and would do surgery again, while 3 declared as unsatisfied with the procedure and would not submit to surgery again. These 3 patients had lower clinical scores and kept complaints related to the original problem but unrelated to donor zone. MRI score significantly improved at 18-24 months comparing with pre-operative ($p = 0.004$). No radiographic or clinical complications related to donor zone with implication in activity were registered.	Larger case series already included. No new safety events.
Figueroa D, Melean P, Calvo R et al. (2011) Osteochondral autografts in full thickness patella cartilage lesions. The Knee 18: 220-3	Case series n=10 FU=8 months	We conclude that patellar OCA is a good alternative for the treatment of full thickness patellar cartilage lesions, offering good clinical, functional and imaging results at midterm follow-up.	Larger case series already included. No new safety events.
Filardo G, Kon E, Di M et al. (2014) Single-plug autologous osteochondral transplantation: results at minimum 16 years' follow-up. Orthopedics 37: e761-7	Case series n=15 FU=16 years	Autologous osteochondral transplantation proved to be, at short-term evaluation, a suitable option to treat small-medium sized chondral and osteochondral lesions. However, clinical improvement is slow and a significant percentage of patients develop symptoms attributable to the donor area, thus reducing the overall benefit of this procedure.	Results reported in paper 3 in table 2.
Filardo G, Kon E, Perdisa F et al. (2014) Autologous osteochondral transplantation for the treatment of knee lesions: results and limitations at two years' follow-up. International orthopaedics 38: 1905-12	Case series n=31 FU=2	A significant increase in Tegner score was seen at the 2-year evaluation, with stable results up to the last follow-up. Four failures were reported, which in 3 cases occurred at mid- to long-term follow-up, confirming that this technique can be considered a suitable option for the treatment of small and medium chondral and osteochondral lesions in young patients.	Results reported in paper 3 in table 2.
Filardo G, Kon E, Perdisa F et al. (2015) Arthroscopic mosaicplasty: long-term outcome and joint degeneration progression. The Knee 22: 36-40	Cases Series n=26 FU=12	Mosaicplasty is an effective surgical option for small lesions of the femoral condyles. Although joint degeneration progression was present at 12 years, this did not affect significantly the clinical outcome which was satisfactory at long-term follow-up.	Results reported in paper 3 in table 2.
Fonseca F and Balaco I (2009) Fixation with autogenous	Case series n=20	The results show that this technique enables the biological fixation of	Larger case series already included.

osteochondral grafts for the treatment of osteochondritis dissecans (stages III and IV). International orthopaedics 33: 139-44	FU=4 years	fragments and, functionally, the clinical results obtained were very good. The osteochondral grafts avoid the implantation of foreign material and make use of bone fragments of the same rigidity as the OCD fragment. We conclude that the technique described is an excellent alternative to the techniques normally used for the fixation of stage III and IV OCD.	No new safety events.
Fonseca F (2009) Mosaicplasty with periosteal graft for resurfacing local full-thickness chondral defects of the knee. Revista brasileira de ortopedia 44:153-8	Case series n=12 FU= 6 years	The mosaicambium technique is an excellent alternative for chondral defects greater than 2 cm2.	Larger case series already included. No new safety events.
Fujita N, Matsumoto T, Kubo S et al. (2012) Autogenous osteochondral graft transplantation for steroid-induced osteonecrosis of the femoral condyle: A report of three young patients. Sports medicine, arthroscopy, rehabilitation, and therapy & technology 4: 13	Case series n=3 FU= 6 to 24 months	Full-thickness cartilage defects sized 20 x 10, 15 x 10, and 30 x 20 mm respectively were classified as International Cartilage Repair Society Grade IV lesions and treated with osteochondral autograft transplantation. They were treated successfully with osteochondral autograft transplantation certificated by post-operative MRI and second look arthroscopy.	Larger case series already included. No new safety events.
Gaweda K, Walawski J, Weglowski R et al. (2006) Early results of one-stage knee extensor realignment and autologous osteochondral grafting. International orthopaedics 30: 39-42	Non-randomised comparative study n=49 FU=24 months	Thirty patients (group I) had chondral defects grade I or II, and 19 patients (group II) had chondral defects grade III or IV. All patients were treated with proximal and distal realignment of the knee extensor mechanism, but group II also had a simultaneous autologous osteochondral grafting of the chondral defect. Patients were followed for 2 years and clinically assessed using the Marshall score comparing the 2 groups. Apart from a slower recovery in group II, the clinical and functional results were almost the same at the final follow-up.	Larger case series already included. No new safety events.
Gilmore CJ, Cosgrove CT, Werner B et al. (2014) Accelerated return to play following osteochondral autograft plug transfer (OATS). Orthopaedic Journal of Sports Medicine 2: no pagination	Case series n=152 FU=3 months	The majority of the patients in this cohort (80%) were cleared to resume athletics by 3 months post OATs procedure. When compared with the current literature on return to play after chondral surgery of the knee1, this represents a greater than 50% more rapid return to full activities in these patients.	Larger case series already included. No new safety events.
Gracitelli GC, Moraes VY, Franciozi CES et al. (2016) Surgical interventions (microfracture, drilling, mosaicplasty, and allograft transplantation) for treating isolated cartilage defects of the knee in adults. Cochrane Database of Systematic Reviews 2016: no pagination	Systematic review n=3 FU=6 to 10 years	The very low quality evidence from RCTs comparing mosaicplasty with microfracture is insufficient to draw conclusions on the relative effects of these 2 interventions for treating isolated cartilage defects of the knee in adults. Of note is that treatment failure, with recurrence of symptoms, occurred with both procedures. Further research is needed to define the best surgical option for treating isolated cartilage	Papers already reported in other papers in table 2. No new safety events.

		defects. We suggest the greatest need is for multi-centre RCTs comparing reconstructive procedures (mosaicplasty versus allograft transplantation) for large osteochondral lesions and reparative procedures (microfracture versus drilling) for small chondral lesions.	
Gudas R, Stankevicius E, Monastyreckiene et al. (2005) Osteochondral autologous transplantation versus microfracture for the treatment of articular cartilage defects in the knee joint in athletes. Knee surgery, sports traumatology, and arthroscopy : official journal of the ESSKA 14: 834-42	RCT n=57 FU=37 months	At an average of 37.1-month follow-up the randomised, clinical study in athletes has shown significant superiority of the OAT over MF for the repair of articular cartilage defects in the knee.	Results reported in papers 1 and 2 in table 2.
Gudas R, Simonaityte R, Cekanauskas E et al. (2009) A prospective, randomized clinical study of osteochondral autologous transplantation versus microfracture for the treatment of osteochondritis dissecans in the knee joint in children. Journal of pediatric orthopedics 29: 741-8	RCT n=50 FU=4	At an average of 4.2-year follow-up, the randomised, clinical study in children under the age of 18 years has shown significant superiority of the mosaic-type OAT over MF for the treatment of osteochondritis dissecans defects in the knee. However, the study has shown that both MF and OAT give encouraging clinical results for children under the age of 18 years.	Results reported in papers 1 and 2 in table 2.
Gudas R, Simonaityte R, Cekanauskas E et al. (2011) Concomitant autologous chondrocyte implantation with osteochondral grafting for treatment of a massive osteochondral defect in the bilateral knees of a child. Medicina (Kaunas, and Lithuania) 47: 170-3	Case report n=1 FU=12	The combination of ACI and OAT methods in a one-step procedure produced a good reconstruction of the joint surface with excellent clinical outcomes in the both knee joints of the same patient. Autologous osteochondral grafting and autologous chondrocyte implantation can be combined for the treatment of large osteochondral defects of the knee.	Larger case series already included. No new safety events.
Gudas R, Gudaite A, Pocius A et al. (2012) Ten-year follow-up of a prospective, randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint of athletes. The American journal of sports medicine 40: 2499-508	RCT n=60 FU=10	The OAT technique for ACD or OCD repair in the athletic population allows for a higher rate of return to and maintenance of sports at the preinjury level compared with MF.	Results reported in papers 1, 2 and 3 in table 2.
Hangody L, Vasarhelyi G, Hangody LR et al. (2008) Autologous osteochondral grafting--technique and long-term results. Injury 39: S32-9	Case series n=383 FU=10 years	According to encouraging results in this increasingly large series, supported by similar findings from other centres, it seems that autologous osteochondral mosaicplasty may be an alternative for small and medium-sized focal chondral and osteochondral defects of weight-bearing surfaces of the knee and other weight-bearing synovial joints.	Results reported in paper 4 in table 2.
Hangody L, Dobos J, Balo E et al. (2010) Clinical experiences with autologous osteochondral	Case series n=413 FU=15 years	Despite a higher rate of preoperative osteoarthritic changes in the athletic patients, clinical outcomes of	Results reported in paper 4 in table 2.

mosaicplasty in an athletic population: a 17-year prospective multicenter study. The American journal of sports medicine 38: 1125-33		mosaicplasty in this group demonstrated a success rate similar to that of less athletic patients. Higher motivation resulted in better subjective evaluation. Slight deterioration in results occurred during the 9.6-year follow-up; thus, autologous osteochondral mosaicplasty may be a useful alternative for the treatment of 1.0- to 4.0-cm(2) focal chondral and osteochondral lesions in competitive athletes.	
Harris J, Hussey K, Saltzman B et al. (2014) Cartilage repair with or without meniscal transplantation and osteotomy for lateral compartment chondral defects. Arthroscopy - Journal of Arthroscopic and Related Surgery 30: e32	Case series n=35 FU=2 years	Statistically significant and clinically meaningful improvements in validated patient-reported clinical outcome scores with minimum 2-year follow-up were seen in 35 subjects having treatment of lateral sided focal chondral defects with or without concomitant lateral meniscus transplant and distal femoral osteotomy. There was a low rate of re-operations and complications.	Larger case series already included. No new safety events.
Hindle P, Hendry JL, Keating JF et al. (2014) Autologous osteochondral mosaicplasty or TruFit plugs for cartilage repair. Knee surgery, sports traumatology, and arthroscopy : official journal of the ESSKA 22: 1235-40	Case series n=66 FU=1 to 5 years	This study demonstrated significantly better outcomes using 2 validated outcome scores (KOOS, EQ-5D), and an ability to return to sport in those having autologous mosaicplasty compared with those having TruFit plugs.	Larger case series already included. No new safety events.
Imade S, Kumahashi N, Kuwata S et al. (2013) A comparison of patient-reported outcomes and arthroscopic findings between drilling and autologous osteochondral grafting for the treatment of articular cartilage defects combined with anterior cruciate ligament injury. The Knee 20: 354-9	Case control n=40 FU=2years	Autologous osteochondral grafting was found to be an effective technique for treating relatively young patients who had cartilage defects combined with ACL injury or OCD, but this technique showed limited results in treating cartilage defects based on advanced patient age and degenerative changes in the cartilage	Larger comparative studies already included. No new safety events.
Karataglis D, Green M A and Learmonth D J. A (2006) Autologous osteochondral transplantation for the treatment of chondral defects of the knee. The Knee 13: 32-5	Case series n=36 FU=37 months	All but 5 patients returned to their previous occupation while 18 went back to sports. No correlation was found between patient age at operation, the size or site of the chondral lesion and the functional outcome. Autologous osteochondral grafting with the OATS technique is a safe and successful treatment option for focal osteochondral defects of the knee. It offers a very satisfactory functional outcome and does not compromise the patient's future options.	Larger case series already included. No new safety events.
Kawano CT, Santos MMR, Oliveira MG et al. (2012) Trapezoidal osteochondral autologous plug single-block graft for treating chondral lesions of the knee: clinical and functional medium-term results	Case series n=25 FU=59 months	Autologous trapezoidal plug single-block grafts are a therapeutic option for defects of varying sizes and provide good clinical results and low morbidity at the donor site in the medium term.	Larger case series already included. No new safety events.

in an observational study. Clinics (Sao Paulo, and Brazil) 67: 1191-5			
Krych AJ, Pareek A, King AH et al. (2016) Return to sport after the surgical management of articular cartilage lesions in the knee: a meta-analysis. Knee Surgery Sports Traumatology Arthroscopy	Meta-analysis n=44 studies FU=18 to 181 months	In conclusion, in this meta-analysis of 2549 athletes, cartilage restoration surgery had a 76 % return to sport at mid-term follow-up. Osteochondral autograft transfer offered a faster recovery and appeared to have a higher rate of return to preinjury athletics, but heterogeneity in lesion size, athlete age, and concomitant surgical procedures are important factors to consider when assessing individual athletes. This study reports on the rate of return to sport in athletes having various procedures for symptomatic chondral defects.	Reported on return to sport. Limited safety and efficacy reported. More comprehensive systematic reviews already in table 2.
Lahav A, Burks RT, Greis PE et al. (2006) Clinical outcomes following osteochondral autologous transplantation (OATS). The journal of knee surgery 19:169-73	Case series n=21 FU=40	Thirteen (86%) patients reported that they would have the surgery again if they had to make the decision a second time. Age did not correlate with subjective results on the IKDC evaluation (P = .7048) or score difference on our questionnaire (P = .9175). This procedure provides an option for articular resurfacing of the femoral condyles for focal areas of chondral defects with promising results regarding subjective improvement.	Larger case series already included. No new safety events.
Leeman JJ, Motamedi D, Wildman-Tobriner B et al. (2016) Intra-articular osteoid osteoma at the femoral trochlea treated with osteochondral autograft transplantation. Journal of radiology case reports 10: 22-29	Case report n=1 FU=6 months	We present the case of an intra-articular osteoid osteoma at the femoral trochlea. Intra-articular osteoid osteoma can present a diagnostic challenge both clinically and with imaging because it presents differently from the classic cortical osteoid osteoma. Given the lesion's proximity to overlying cartilage, the patient had resection of the lesion with osteochondral autograft transplantation at the surgical defect. A comprehensive literature review and discussion of intra-articular osteoma will be provided.	Larger case series already included. No new safety events.
Li Z, Zhu T and Fan W (2016) Osteochondral autograft transplantation or autologous chondrocyte implantation for large cartilage defects of the knee: a meta-analysis. Cell and tissue banking 17: 59-67	Meta-analysis n=5 RCTs FU=12 to 120 months	In the 6 comparisons of excellent or good results and poor results, the outcomes of ACI were significantly better than OAT in only 1 comparison (RR 2.57, 95 % CI 1.09-6.07, P = 0.03) while others had no significant differences. We may reach a primary conclusion that there is no significant different outcome between ACI and OAT in a short-term follow-up but it may indicate that the patients with OAT may be more likely to have worse condition than that with ACI for a long-term period.	Relevant studies already reported in paper 1 in table 2.
Lintz F, Pujol N, Pandeirada C et al. (2011) Hybrid fixation: evaluation of a novel technique in adult osteochondritis	Case series n=7 FU=27	Isolated screw fixation of osteochondritis dissecans in adults provides poor bony integration. Mosaicplasty is an alternative but does	Larger case series already included. No new safety events.

dissecans of the knee. Knee surgery, sports traumatology, and arthroscopy : official journal of the ESSKA 19: 568-71		not retain normal condylar anatomy. The hybrid fixation technique adds a biological "booster" to osteochondritis fixation, with excellent short-term outcome. Further studies are needed to investigate the long-term results.	
Lonner JH, Mehta S, Booth RE et al. (2007) Ipsilateral patellofemoral arthroplasty and autogenous osteochondral femoral condylar transplantation. The Journal of arthroplasty 22: 1130-6	Case series n=4 FU=2.7 years	The mean patellofemoral pain score improved from 12 to 49, and the patellofemoral function score increased from 16 to 42. There have been no radiographic signs of progressive tibiofemoral cartilage degeneration. Combining patellofemoral arthroplasty and autologous osteochondral transplantation is a reasonable short-term approach to this condition.	Larger case series already included. No new safety events.
Lu AP and Hame SL (2005) Autologous osteochondral transplantation for simple cyst in the patella. Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 21: 1008	Case series n=1 FU=3 months	Treatment options for chondral and osteochondral defects of the patella have been few and results have been inconsistent at best. Autologous osteochondral transplantation presents a new way to revisit these patellar defects. We report the case of a young female softball player with a simple cyst in the patella and an osteochondral defect that serves as the indication for autograft osteochondral transplantation.	Larger case series already included. No new safety events.
Marcacci M, Kon E, Delcogliano M et al. (2007) Arthroscopic autologous osteochondral grafting for cartilage defects of the knee: prospective study results at a minimum 7-year follow-up. The American journal of sports medicine 35: 2014-21	Case series n=30 FU=7 years	The results of this technique at medium- to long-term follow-up are encouraging. This arthroscopic 1-step surgery appears to be a valid solution for treatment of small, grade III to IV cartilage defects.	Larger case series already included. No new safety events.
Maruyama M, Takahara M, Harada M et al. (2014) Outcomes of an open autologous osteochondral plug graft for capitellar osteochondritis dissecans: time to return to sports. The American journal of sports medicine 42: 2122-7	Case series n=33 FU=28	The results of this study indicate that an open autologous osteochondral plug graft allows a return to the previous competitive level of throwing by a mean of 7 months postoperatively.	Larger case series already included. No new safety events.
Miniaci A and Tytherleigh-Strong G (2007) Fixation of unstable osteochondritis dissecans lesions of the knee using arthroscopic autogenous osteochondral grafting (mosaicplasty). Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 23: 845-51	Case series n=20 FU=18 months	Autogenous osteochondral grafting of unstable OCD lesions in the knee is a reliable and minimally invasive technique that provides a stable biologic fixation using autogenous bone graft and has few complications.	Larger case series already included. No new safety events.
Miura K, Ishibashi Y, Tsuda E et al. (2007) Results of	Case series n=12	Biological fixation of the osteochondral dissecans lesion with cylindrical	Larger case series already included.

arthroscopic fixation of osteochondritis dissecans lesion of the knee with cylindrical autogenous osteochondral plugs. The American journal of sports medicine 35: 216-22	FU=4.5 years	osteochondral autograft provided healing of the osteochondral fragments.	No new safety events.
Muller S, Breederveld RS and Tuinebreijer WE (2010) Results of osteochondral autologous transplantation in the knee. The open orthopaedics journal 4: 111-4	Case series n=14 FU=42 months	The OATS-technique resulted in a decrease in symptoms in patients with localized articular cartilage defects. We consider the OATS technique to be an appropriate treatment for cartilage defects to prevent progression of symptoms.	Larger case series already included. No new safety events.
Nakagawa Y, Suzuki T, Kuroki H et al. (2007) The effect of surface incongruity of grafted plugs in osteochondral grafting: a report of five cases. Knee surgery, sports traumatology, and arthroscopy : official journal of the ESSKA 15: 591-6	Case series n=5 FU=32	Second-look arthroscopy showed that the depressed areas were covered with fibrocartilage-like tissue, and that the joint surface was smooth. In conclusion, our clinical results and second-look arthroscopic evaluation suggest that isolated osteochondral plug depressions of not greater than 1 mm could still promote acceptable cartilage healing leading to good clinical outcomes. However, plug protuberance at mosaicplasty should always be avoided.	Larger case series already included. No new safety events.
Naveen S, Robson N and Kamarul T (2011) Comparative analysis of autologous chondrocyte implantation and other treatment modalities: a systematic review. European Journal of Orthopaedic Surgery and Traumatology , 1-8	Systematic review n=4 RCTs FU=19 to 36 months	Despite significant differences between the methodologies employed by different researchers, we can conclude that all except 2 studies demonstrated ACI being the better treatment for cartilage defects. However, final conclusions regarding long-term effects are still difficult, and therefore, future studies are needed to answer the long-term effects of ACI.	More comprehensive systematic reviews already in table 2.
Nho SJ, Foo LF, Green DM et al. (2008) Magnetic resonance imaging and clinical evaluation of patellar resurfacing with press-fit osteochondral autograft plugs. The American journal of sports medicine 36: 1101-9	Case series n=22 FU=28 months	Patellar AOT is an effective treatment for focal patellar chondral lesions, with significant improvement in clinical follow-up. This study suggests that patients with patellar malalignment may represent a subset of patients who have a poor prognostic outlook compared with patients with normal alignment.	Larger case series already included. No new safety events.
Nishimura A, Morita A, Fukuda A et al. (2011) Functional recovery of the donor knee after autologous osteochondral transplantation for capitellar osteochondritis dissecans. The American journal of sports medicine 39: 838-42	Case series n=12 FU=24 months	A time lag was evident in recovery between postoperative symptoms and muscle power at 3 months. However, harvesting osteochondral grafts did not exert adverse effects on donor knee function in young athletes at 2 years after having osteochondral autograft transplantation for capitellar osteochondritis dissecans.	Larger case series already included. No new safety events.
Okamoto Y, Nakagawa Y, Maekawa M et al. (2007) Osteochondral grafting for treatment of a massive chondral defect in the knee of a young adult with anterior cruciate ligament deficit.	Case report n=1 FU=3 years	Follow-up examination, done 36 months after surgery, has shown an excellent result, with a Lysholm score of 100, an International Knee Documentation Committee score of 95.4, and full range of knee motion with no symptoms. Plain radiographs at that	

Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 23: e1-4		time showed preservation of the medial joint space on the weighted anteroposterior view. No osteoarthritic changes were evident in the patellofemoral joint.	
Onoda S, Sugita T, Aizawa T et al. (2012) Osteochondritis dissecans of the knee in identical twins: a report of two cases. Journal of orthopaedic surgery (Hong Kong) 20: 108-10	Case series n=2 FU=2 months	We report the second case of osteochondritis dissecans (OCD) of the knee in identical twins (bilaterally in one and unilaterally in the other). Fixations with bio-absorbable pins, cylindrical osteochondral graft, and osteochondral mosaicplasty were all successful and bone union was achieved. We considered that genetic factors remain essential even if other factors (particularly repetitive trauma) are mainly responsible for the occurrence of OCD.	Larger case series already included. No new safety events.
Ovesen J, Olsen BS and Johannsen HV (2011) The clinical outcomes of mosaicplasty in the treatment of osteochondritis dissecans of the distal humeral capitellum of young athletes. Journal of shoulder and elbow surgery 20: 813-8	Case series n=10 FU=30 months	Autologous osteochondral mosaicplasty for advanced lesions of capitellar osteochondritis dissecans can provide satisfactory clinical and radiographic results.	Larger case series already included. No new safety events.
Ozturk A, Ozdemir MR and Ozkan Y (2006) Osteochondral autografting (mosaicplasty) in grade IV cartilage defects in the knee joint: 2- to 7-year results. International orthopaedics 30: 200-4	Case series n=19 FU=32	Magnetic resonance imaging (MRI) examination at the last follow-up visit revealed that congruency was restored in 16 (84.2%) without any signs of fissuring or delamination but in 3 patients (15.8%) a 1-mm difference between graft and recipient surface was detected. No complications were seen in the patients. Mosaicplasty is a really effective method of treatment for grade IV cartilage lesions in the knee joint.	Larger case series already included. No new safety events.
Panics G, Hangody LR, Balo E et al. (2012) Osteochondral Autograft and Mosaicplasty in the Football (Soccer) Athlete. Cartilage 3: 25S-30S	Case series n=61 FU=10 years	Autologous osteochondral mosaicplasty in competitive football players is a good alternative procedure to repair cartilage damage.	Reported in paper 3 in table 2.
Pareek A, Reardon PJ, Macalena JA et al. (2016) Osteochondral Autograft Transfer Versus Microfracture in the Knee: A Meta-analysis of Prospective Comparative Studies at Midterm. Arthroscopy - Journal of Arthroscopic and Related Surgery 32: 2118-2130	Meta-analysis n=6 studies FU=10 years	Overall, OAT showed successful outcomes in 72% of patients at long-term follow-up. Increased age, previous surgery, and defect size correlated positively with failure rate, whereas success improved with concomitant surgical procedures. Nonetheless, this systematic review is limited by heterogeneity in a surgical technique, lesion and patient characteristics, and reporting of non-standardised outcome measures.	More comprehensive meta-analysis already included in table 2.
Pascual-Garrido C, Friel NA, Kirk SS et al. (2009) Midterm results of surgical treatment for adult osteochondritis dissecans	Non-randomised comparative study	Patients with adult osteochondritis dissecans of the knee, treated with surgical cartilage procedures, show durable function and symptomatic	Larger case series already included. No new safety events.

of the knee. The American journal of sports medicine 37: 125S-30S	n=46 FU=4	improvement at a mean 4.0 years of follow-up. Patients treated with arthroscopic reduction and internal fixation and loose-body removal demonstrated a greater improvement in outcome scores than those treated with osteochondral allograft.	
Pascual-Garrido C, Daley E, Verma NN et al. (2016) A Comparison of the Outcomes for Cartilage Defects of the Knee Treated With Either Biologic Resurfacing Versus Focal Metallic Implants. Arthroscopy - Journal of Arthroscopic and Related Surgery , no pagination	Non-randomised comparative study n=46 FU=4 years	Careful patient selection can achieve high satisfaction rates with both biological and focal metal resurfacing procedures for the treatment of isolated focal chondral lesions of the femoral condyle in the knee. Focal metallic resurfacing results in similar clinical outcomes and provides excellent success rates at short-term follow-up.	Studies with higher level of evidence already included. No new safety events.
Quarch VMA, Enderle E, Lotz J et al. (2014) Fate of large donor site defects in osteochondral transfer procedures in the knee joint with and without TruFit plugs. Archives of orthopaedic and trauma surgery 134: 657-66	Non-randomised comparative study n=37 FU=2 years	OCT is an effective therapy even for large chondral defects >3 cm. By filling the defects with TruFit implants, no clinical improvements could be found since the donor site morbidity was already low anyway. However, the regeneration of defects filled with TruFit implants took more than 2 years.	Studies with higher level of evidence already included. No new safety events.
Reverte-Vinaixa MM, Joshi N, Diaz-Ferreiro EW et al. (2013) Medium-term outcome of mosaicplasty for grade III-IV cartilage defects of the knee. Journal of orthopaedic surgery (Hong Kong) 21: 4-9	Case series n=17 FU=7 years	At year 7, MRI showed good integration of the implant in all 11 available patients, but fissures were seen on the cartilage surface in 3 patients, CONCLUSION: The medium-term outcome of autologous mosaicplasty for symptomatic osteochondral defects in the femoral condyle is good.	Larger case series already included. No new safety events.
Robb CA, El-Sayed C, Matharu GS et al. (2012) Survival of autologous osteochondral grafts in the knee and factors influencing outcome. Acta orthopaedica Belgica 78: 643-51	Case series n=55 FU=6years	Linear regression analysis demonstrated an improved outcome in Oxford knee score in younger patients. Gender, BMI, previous or associated knee surgery, site and size of the graft had no influence on outcome. The authors consider autologous osteochondral grafting as a reliable method of treatment in the medium-term for young patients with small contained articular cartilage lesions up to 4 cm2. Careful attention should be paid to the mechanical axis (varus) before grafting. Long-term studies are necessary.	Larger case series already included. No new safety events.
Ronga M, Stissi P, La B et al. (2015) Treatment of unstable osteochondritis dissecans in adults with autogenous osteochondral grafts (Mosaicplasty): long-term results. Joints 3: 173-8	Case series n=4 FU=10 years	The fixation of large and unstable OCD lesions with mosaicplasty may be a good option for treating type II or III OCD lesions in adults. The advantages of this technique include stable fixation, promotion of blood supply to the base of the OCD fragment, and grafting of autologous cancellous bone that stimulates healing with preservation of the articular surface.	Larger case series already included. No new safety events.
Rose T, Craatz S, Hepp P et al. (2005) The autologous osteochondral transplantation of the knee: clinical results,	Case series n=27 FU=14 months	The congruency of the joint surface cannot be restored to the original status, particularly in larger defects with irregular shapes. However, we did not	Larger case series already included. No new safety events.

radiographic findings and histological aspects. Archives of orthopaedic and trauma surgery 125: 628-37		find any aspects which affected the function of the knee joint following OCT. It can be assumed that remaining lesions at the surrounding cartilage could maintain the inflammatory process and therefore maintain the pain and a low knee function. Further investigations are needed to specify the effects of the OCT on the transplanted cartilage and its influence on the later clinical outcome.	
Sasaki K, Matsumoto T, Matsushita T et al. (2012) Osteochondral autograft transplantation for juvenile osteochondritis dissecans of the knee: a series of twelve cases. International orthopaedics 36: 2243-8	Case series n=12 FU=26 months	OAT for JOCD of the knee provided satisfactory results in all patients at a mean follow-up of 26.2 months.	Larger case series already included. No new safety events.
Smolders JMH, Kock NB, Koeter S et al. (2010) Osteochondral autograft transplantation for osteochondritis dissecans of the knee. Preliminary results of a prospective case series. Acta orthopaedica Belgica 76: 208-18	Case series n=7 FU=1 year	Mosaic OAT appeared in this study as a valid treatment option in selected cartilage defects. OCD lesions improved significantly following osteochondral transplantation. The limitations of this technique are the number and size of the plugs needed to repair the defect. Future research should focus on identifying the appropriate choice of operative treatment for well-defined subtypes of articular cartilage lesions, rather than searching for 1 superior technique for all.	Larger case series already included. No new safety events.
Solheim E, Hegna J, Oyen J et al. (2013) Results at 10 to 14 years after osteochondral autografting (mosaicplasty) in articular cartilage defects in the knee. The Knee 20: 287-90	Case series n=73 FU=10 years	We conclude that the long-term clinical outcome after mosaicplasty varies greatly depending on age, gender and the size of the lesion.	Larger case series already included. No new safety events.
Ulstein S, Aroen A, Rotterud JH et al. (2014) Microfracture technique versus osteochondral autologous transplantation mosaicplasty in patients with articular chondral lesions of the knee: a prospective randomized trial with long-term follow-up. Knee surgery, sports traumatology, and arthroscopy : official journal of the ESSKA 22: 1207-15	RCT n=25 FU=10	At long-term follow-up, there were no significant differences between patients treated with MF and patients treated with OAT mosaicplasty in patient-reported outcomes, muscle strength or radiological outcome.	Reported in papers1, 2 and 3 in table 2.
Unnithan A, Jimulia T, Mohammed R et al. (2008) Unique combination of patellofemoral joint arthroplasty with Osteochondral Autograft Transfer System (OATS) - a case series of six knees in five patients. The Knee 15: 187-90	Case series n=6 FU=4 years	We present our case series of 6 knees in 5 patients where we combined the 2 procedures and extended the indication for PFA and delayed the need for total knee arthroplasty (TKA) in all but 1 patient over a mean follow up period of 3.8 years.	Larger case series already included. No new safety events.
Visona E, Chouteau J, Aldegheri R et al. (2010)	Case series n=6	Osteochondral grafting with the mosaicplasty technique has been	Larger case series already included.

Patella osteochondritis dissecans end stage: The osteochondral mosaicplasty option. Orthopaedics & traumatology, and surgery & research : OTSR 96. 543-8	FU=26	shown to be effective and give satisfying functional results. The problem of the per-operative cylindrical bone plugs choice needs to be addressed during the procedure course itself, according to the patella lesion location.	No new safety events.
Wajid MA, Shah MI, Mohsin A et al. (2011) Osteochondral grafting of knee joint using mosaicplasty. Journal of the College of Physicians and Surgeons-Pakistan : JCPSP 21: 184-6	Case report n=1 FU=2 years	A young man had this procedure for recalcitrant knee pain at our institution. At 2-year follow-up, his knee pain has significantly improved. We hereby present medium term results (2 years) of this first case report in local literature.	Larger case series already included. No new safety events.
Wajsfisz A, Makridis KG and Djian P (2013) Arthroscopic retrograde osteochondral autograft transplantation for cartilage lesions of the tibial plateau: a prospective study. The American journal of sports medicine 41: 411-5	Case series n=4 FU=55 months	Treatment of tibial plateau cartilage defects with arthroscopic retrograde osteochondral autograft transplantation could be done on a routine basis in clinical practice. The results were encouraging and showed good incorporation of the graft, a minimal failure rate, and satisfactory functional outcomes of patients.	Larger case series already included. No new safety events.
Wang C J (2013) Autologous osteochondral graft for focal articular cartilage defect of the knee. Arthroscopy - Journal of Arthroscopic and Related Surgery 29: e50-e51	Case series n=25 FU= 2 to 7 years	Autologous osteochondral graft provides good or excellent results in 85% of patients with focal contained chondral and osteochondral defects of the knee. There was no correlation of the clinical results with the nature of the disease and the size of the lesion smaller than 500 mm2. Any lesion larger than 500 mm2 is prone to poor clinical outcome. Autologous osteochondral graft is suitable for treatment of knee with moderate size full thickness contained articular cartilage defect of the knee.	Larger case series already included. No new safety events.
Widuchowski W, Lukasik P, Kwiatkowski G et al. (2008) Isolated full thickness chondral injuries. Prevalance and outcome of treatment. A retrospective study of 5233 knee arthroscopies. Acta chirurgiae orthopaedicae et traumatologiae Cechoslovaca 75: 382-6	Case series n=5233 FU=1 to 7 years	Treatment of isolated deep chondral lesions of the knee remains a questionable issue. Little invasive arthroscopic methods as well as using no surgical treatment in grade 3 and 4 isolated cartilage lesions may be effective and improve symptoms and knee function at mid-term follow-up. Data support also the contention that the natural history of cartilage lesions still remains unpredictable and not well understood.	NO subgroup analysis is possible for mosaicplasty.
Yamamoto Y, Tsuda E, Maeda S et al. (2013) Mid-term results of biological fixation with autogenous osteochondral plugs for osteochondritis dissecans lesion of the knee. Arthroscopy - Journal of Arthroscopic and Related Surgery 29: e162	Case series n=21 FU=8 years	No complications arising from the donor site area were seen. Biological fixation of unstable OCD lesions with osteochondral autografts provided reliable mid-term clinical outcome. Age but not preoperative osteochondral condition at the time of surgery may influence knee related QOL at final follow up.	Larger case series already included. No new safety events.
Zak L, Krusche-Mandl I, Aldrian S et al. (2014) Clinical and MRI evaluation of medium- to long-term results after autologous	Case series n=10 FU=7 years	. Long-term results after OCT reflect an impairment in clinical scores in the first 2 years with good results during follow-up. Stable conditions were seen	Larger case series already included. No new safety events.

osteochondral transplantation (OCT) in the knee joint. Knee surgery, sports traumatology, and arthroscopy : official journal of the ESSKA 22: 1288-97		between 2 and 7 years after surgery. The filling of the defects and the cartilage interface appeared good at MRI evaluation after the first 2 years, but cartilage loss was seen between the medium- and long-term follow-ups. Isotropic imaging with multiplanar reconstruction is useful for daily clinical use to assess bony cylinders in cartilage repair, especially in combination with the 3D MOCART.	

Literature search strategy

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	11/01/2017	Issue 1 of 12, January 2017	2
HTA database (Cochrane)	11/01/2017	Issue 4 of 4, October 2016	9
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane)	11/01/2017	Issue 11 of 12, November 2016	62
MEDLINE (Ovid)	11/01/2017	1946 to December week 1	648
MEDLINE In-Process (Ovid)	11/01/2017	January 10, 2017	151
EMBASE (Ovid)	11/01/2017	1974 to 2017 January 10	1218
PubMed	11/01/2017	-	29
BLIC (British Library)	11/01/2017	-	5

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

Database: Medline
Database: Ovid MEDLINE(R) <1946 to December Week 1 2016> Search Strategy: --- 1 Knee Joint/ (52566) 2 Knee Injuries/ (19880) 3 knee*.tw. (115177) 4 Patella/ (10833) 5 patella*.tw. (17464) 6 trochlea*.tw. (3140) 7 ((medial or lateral) adj4 condyle*).tw. (3899) 8 or/1-7 (142598) 9 exp Osteochondritis/ (8358) 10 ((chondral or osteochondral or chondrocyt* or chondroblast* or osteochondriti*) adj4 (defect* or damag* or injur* or lesion*)).tw. (4678) 11 exp Cartilage Diseases/ (14205) 12 (cartilage adj4 disease*).tw. (1246) 13 chondropath*.tw. (353) 14 Weight-bearing/ (18957) 15 (weight-bearing or weightbearing or weight bearing).tw. (13301) 16 or/9-15 (48501) 17 cartilage, articular/ or Hyaline Cartilage/ (30638) 18 cartilage.tw. (72411) 19 Chondrocytes/ (16425) 20 chondrocyte*.tw. (25976)

21 or/17-20 (89490)
22 Transplantation, Autologous/ (50148)
23 (autologous or autogenous or autograft or autotransplant* or auto-transplant*).tw. (99202)
24 Bone Transplantation/ (30522)
25 (bone* adj4 transplant*).tw. (39225)
26 Autografts/ (1736)
27 or/22-26 (176079)
28 8 and 16 and 21 and 27 (1049)
29 mosaic*.tw. (34209)
30 (OATS or COR).tw. (9537)
31 29 or 30 (43724)
32 8 or 16 (179144)
33 31 and 32 (388)
34 28 or 33 (1289)
35 Autogenous Osteochondral Grafting System.tw. (0)
36 AOGS.tw. (9)
37 Osteochondral Autograft Transfer system.tw. (32)
38 Chondral Osseous Replacement.tw. (1)
39 or/34-38 (1309)
40 animals/ not humans/ (4782110)
41 39 not 40 (1022)
42 limit 41 to english language (877)
43 (200512* or 2006* or 2007* or 2008* or 2009* or 201*).ed. (9790319)
44 42 and 43 (648)

Notes:

Record any important decisions on how the strategy was developed

Tested including Femur terms but this returned a lot of results on hip mosaicplasty