



■ SYSTEMATIC REVIEW

A systematic review of surgical methods to restore articular cartilage in the hip

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This systematic review examines the current literature regarding surgical techniques for restoring articular cartilage in the hip, from the older microfracture techniques involving perforation to the subchondral bone, to adaptations of this technique using nanofractures and scaffolds. This review discusses the autologous and allograft transfer systems and the autologous matrix-induced chondrogenesis (AMIC) technique, as well as a summary of the previously discussed techniques, which could become common practice for restoring articular cartilage, thus reducing the need for total hip arthroplasty. Using the *British Medical Journal* Grading of Recommendations, Assessment, Development and Evaluation (BMJ GRADE) system and Grade system. Comparison of the studies discussed shows that microfracture has the greatest quantity and quality of research, whereas the newer AMIC technique requires more research, but shows promise.

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Article focus

- This article focuses on the different surgical methods available to restore articular cartilage in hips.
- This article shows what method appears to be best for restoring articular cartilage and our reasons for it. This is backed up by a full literature review showing the different clinical trials that have been done regarding the techniques.
- Finally we highlight where research should now be aimed.

Key messages

- There is an abundance of research into the microfracture technique but they all show the same floor. There is some relief of symptoms however this only lasts a short duration in time due to type 1 collagen formation not the natural type 2.
- The work done using the AMIC shows it to have great potential.
- The potential of coupling cell therapies to scaffolds has strong potential and could be a potential line of enquiry.

Strengths and limitations

- There are several studies with long follow up periods and large cohort sizes for

different methods especially in regards to microfracture. The longevity of the studies is of benefit as they allow us to see long term benefits of the techniques.

- There are some studies with short follow up periods and small cohort sizes. These may mask some pitfalls in their techniques, especially when evaluating the long-term success of the technique in question.
- There are different scoring systems used to measure the efficacy of the studies. This can lead some difficulty in comparing different studies and techniques against each other.

Introduction

The cause of symptomatic hip pain in the young population is commonly due to a labral tear.¹ These tears often occur anteriorly, and are frequently associated with chondral lesions and early-onset osteoarthritis (OA) secondary to impingement disorders.^{2,3} Inheritance patterns have been identified in OA upon examination of concordance rates between monozygotic (MZ) and dizygotic (DZ) twins, and show increased incidence in MZ. OA does not simply result from exposure to environmental factors such as body weight.² Similarly, genetic influence has been

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noted in impingement disorders of the hip.⁴ Whether this information can be used in the future to identify and treat these problems early, remains to be seen.

Once chondral cartilage is lost, there are few current surgical measures available that aim to restore the cartilage, making the need for total hip arthroplasty (THA) seem inevitable. However, arthroscopic techniques have evolved, allowing us to perform interventions which initially would not be possible because of technical limitations. The procedures available range from microfracture to cartilage scaffold. The last review on hip cartilage regeneration was performed in 2012.⁵ We therefore felt the need to perform an update of the literature to see if the results favour any one particular method.

We found several gaps in the literature regarding surgical techniques to manage chondral defects during arthroscopy, and this provided the starting point for our review: to outline and evaluate the gaps in the literature using the Grade⁶ guidelines.

Materials and Methods

On 26 June 2017, we performed a PubMed search using the keywords ‘hip’, ‘cartilage’, ‘regeneration’ and ‘surgery’. This returned 115 papers, but only 14 were deemed relevant (review papers and those referring to the knee were excluded). These 14 papers were evaluated using the Grade⁶ guidelines. The GRADE system is used as a method to grade studies against each other in terms of methodological floors, generalizability to the public, effectiveness of treatment, and consistency with other studies, and have also devised a system of categorizing studies according to the level of evidence (from 1⁺⁺ to 4) and classification of recommendation (A to D) (Tables I and II).

Surgical techniques: microfracture. This is the oldest technique for cartilage restoration in weight-bearing regions of the joint, performed in over 1800 patients.⁷ Unfortunately, only a small proportion of these were in the hip and these were on lesions smaller than 4 cm².^{7,8} This surgery is low in complexity with a low risk of associated patient morbidity.⁷

The operation involves specially designed awls perforating the subchondral bone of the femoral head or the acetabulum. The perforations are made as close together as possible, while ensuring they do not infringe and ‘rupture into’ each other. The perforations are normally 2 mm deep, as deeper holes show no significant effect on cartilage production, but may reduce the integrity of the subchondral bone and cause osteocyte necrosis.⁷⁻¹⁰

Immediately, a blood clot rich in stem cells is formed, leading to fibrocartilage production, not the original hyaline.¹¹ Fibrocartilage is less flexible, and may explain why pain relief following surgery is limited to approximately five years.⁸

Following this, McGill et al⁸ undertook a two-year follow-up of 21 hip microfracture surgeries. This study did not investigate the success of the surgery; rather, it showed surgery was technically possible without causing harm to the patient. These data were unpublished.

Philippon et al¹² showed that in a 20-month period, the mean fill of acetabular chondral lesions was 91%, however, the scope of results between patients varied from 25% to 100%. Concerns were that there was no comparison group, the ages were not stated, and there were only nine participants.

Through observations in mammalian models, microfracture of the acetabulum leads to an increase in type II collagen micro RNA (mRNA) after six weeks. This looked promising, however, mRNA does not always lead to more protein, and there was no significant increase in other Extra Cellular Matrix (ECM) products such as aggrecan.¹¹

Unfortunately, an animal study has shown strong evidence for bone cyst formation.¹⁰ Bone cysts are common markers for OA.¹³ However, we found no documented human cases, possibly because the cyst formation is being accredited to the chondral lesion rather than to the surgery.

The effectiveness of microfracture is highly disputed. McDonald’s¹⁴ case control study of young male athletes returning to sport following microfracture surgery showed no significant improvements over those who did not undergo surgery (77% vs 88%).¹⁴ Of concern with McDonald’s case control study, is the patient group: they are male, young and active, and thus have better recovery time with or without the surgery due to the rest period.

An important study by Byrd and Jones¹⁵ examined 220 patients undergoing hip arthroscopy for CAM impingement. All patients showed improvements, however, there was no difference between those undergoing microfracture surgery and those not. Despite the large study population, only 58 hips underwent microfracture surgery. There was no loss to follow-up. Nevertheless, given the inclusion of a comparison group, this study holds the advantage over others.

Haviv’s¹⁶ similar study involved 381 patients with acetabular chondral defects, of whom only 29 had microfracture surgery. These patients did have a mean improvement in modified Harris Hip Scores (mHHS) and Non-Arthritic Hip Scores, however, patient scores were not statistically significant. Perhaps with a larger study and a smaller loss to follow-up, there could be a statistically significant improvement. These large studies, showing little impact and possible bone cyst formation, explain why microfracture is not currently a common surgical method.

There is strong evidence for this technique above, and it is used commonly in other joints. We would recommend using this technique on chondral lesions of size no greater

Table I. Levels of evidence

Level of evidence	Type of evidence
1 ⁺⁺	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCT), or RCT with a very low risk of bias
1 ⁺	Well-conducted meta-analyses, systematic reviews of RCT, or RCT with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews of RCT, or RCT with a high risk of bias
2 ⁺⁺	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2 ⁺	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2 ⁻	Case-control or cohort studies with a high risk of confounding bias, or chance and significant risk that the relationship is not causal
3	Non-analytic studies (for example, case reports, case series)
4	Expert opinion, formal consensus

Table II. Classification of recommendations

Class	Evidence
A	At least one meta-analysis, systematic review, or randomized controlled trial (RCT) that is rated as 1 ⁺⁺ , and is directly applicable to the target population, or a systematic review of RCT or a body of evidence that consists principally of studies rated as 1 ⁺ , is directly applicable to the target population and demonstrates overall consistency of results. Evidence drawn from a NICE technology appraisal
B	A body of evidence that included studies rated as 2 ⁺⁺ , is directly applicable to the target population and demonstrates overall consistency of results, or extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺
C	A body of evidence that includes studies rated as 2 ⁺ , is directly applicable to the target population and demonstrates overall consistency of results, or extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4, or extrapolated evidence from studies as 2 ⁺ , or formal consensus
D (GPP)	A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

than 5 cm². Review scores, level of evidence =2, classification of evidence C.

Transfer systems: autologous chondrocyte implantation. A small plug of cartilage (approximately 5 cm²) from the periphery of the joint is transplanted to a damaged area following *in vitro* culturing in order to maximize the size available for covering the cartilage defect.¹⁷

Autologous chondrocyte implantation (ACI) is performed via arthroscopy and is therefore minimally invasive. Following access via incision, the size of the cartilage lesions and the size and quantity of grafts required are calculated. The chondrocytes are expanded *in vitro*. Two operations are required: harvesting and implantation.

A study on rabbits showed that the healing potential of cartilage was significantly worse in the peripheral, non-weight-bearing regions of the joint from which it is harvested compared with the weight-bearing regions. This suggests that it may not be as efficient as cartilage taken from the weight-bearing regions, such as in allografts.¹⁸ There is a case study¹⁹ of a 19-year-old female patient who underwent ACI on a 10 cm² chondral defect. The patient has been pain-free for two years.¹⁹ Another paper involved 14 patients where 71% showed improvements after one year.²⁰ These two studies have shown that ACI can be used in the hip with positive results - Review scores, level of evidence = 3 classification = D.

Transfer systems: allografts. This involves the replacement of hyaline cartilage from non-self joints. It holds several advantages over autografts, including reduced morbidity in the graft site and the potential acquisition of a larger 'plug', up to the size of 15 cm², thus larger

chondral defects can be refurbished.²¹ Compared with autografts, hyaline cartilage from a site near-identical to that of the chondral defect can be used.²² This was first performed in the hip by Krych et al²³ in 2011.

Following transplantation, chondrocytes can support the cartilage matrix, including the ECM,²⁴ thereby overcoming some of the issues previously identified with the microfracture technique. Due to their location in the ECM, chondrocytes are immunoprivileged.^{24,25} Therefore, unlike with organ transplants, human leukocyte antigen matching is not necessary. It is possible to perform multiple allograft transplants from one donor joint.

When transplanting cartilage, processing and procurement is carried out according to the American Association of Tissue Banks (AATB) guidelines.²⁶ Before the transfer of bodily fluids, extensive testing should be carried out to prevent disease transfer, however, there have been several documented disease transmissions.²⁷

The natural ageing of cartilage, especially in the hip, means the use of older donors is not always viable. There is no need for tissue typing, but the availability of high-quality hyaline cartilage for certain joint areas is limited.

The first surgeries were in 2011, when both a male and female patient had osteochondral deficits in the hip. Following surgery, both had reduced hip pain until the end of follow-up (3.5 years).²³ However, this was a very small cohort size and lifetime follow-up would have been logistically simple. A later study by Khanna et al²⁸ did exactly what was needed; a mixed gender cohort of 17 participants followed up for a mean of 42 months. There

was a significant drop-out due to a large geographical distribution, but seven of the patients had good results, six had fair results and four had poor results. Despite some people being given a 'poor' result, when comparing the patients' final HHS with the preoperative score, only one patient's score decreased.

There is limited evidence on this technique, nonetheless, it can work, and allografts could be a method for restoring larger chondral defects - Review scores level of evidence = 3 classification = D

Mosaicplasty. Mosaicplasty evolves from autografts. Several small plugs are taken, not just one. One study observed femoral heads with cartilage damage undergoing osteochondral mosaicplasty.²⁹ There was vast improvement in range of movement and pain scores. Radiological follow-up showed strong and stable femoral heads with smooth articular cartilage. However, it has the same pitfalls as autografts, but there is only one long-term (> 5 years) follow-up in the hip.²⁹

The use of this technique is not currently recommended due to the low level of evidence. Any further successful research into autograft surgery can only increase the use of mosaicplasty - Review scores, level of evidence = 2- classification = D

Synthetic osteochondral plug. This is a novel method of restoring cartilage which involves making a tunnel from the iliac crest region to the roof of the acetabulum and placing the graft. A study from Field et al³⁰ reported that after a mean ten-month follow-up period, all patients showed improvements, and radiological imaging showed that the plug was still stable. However, the patient population was very small, with only four participants. There was no comparison group and follow-up time was only ten months. The longevity of the plug's stability is unknown compared with hip arthroplasty, however, physiologically, repeat surgeries could go ahead. Review scores, level of evidence = 3 classification = D

Synthetic scaffold resurfacing. This is where a synthetic graft or scaffold is soaked in a stem cell-rich solution before insertion into the damaged joint.

These scaffolds are cylindrical plugs, composed of biodegradable materials such as polylactide-co-glycolide, calcium sulphate, and polyglycolide fibres. They have different mechanical functions, dependant upon their final position. The deeper layer has mechanical properties which resemble the subchondral bone, whereas superficial layers mimic hyaline cartilage.

Fat-derived stem cells, which have been grown on a 3D scaffold of the same shape as a hip joint, have been shown both to maintain shape and form cartilage. A team at Duke University³¹ initially engineered a scaffold that was able to 'chaperone' stem cells to chondrocytes.

The 3D scaffold can be manipulated and moulded to mimic the shape of the joint surface. The fat-derived cells

are obtained via liposuction and require 38 days to cover the scaffold fully. This is a very recent discovery, thus no clinical trials have been found.³¹

Kreuz et al³² investigated the use of infant chondrocytes to regenerate articular cartilage with the support of a scaffold. Hip cartilage was taken from children aged between one and ten years old, and cultured in polyglycolic acid scaffolds. The results were promising, but have limited worth, as the cartilage was transplanted into mice. This is, nevertheless, a viable avenue to explore.

In 2011, Wang et al³³ demonstrated the use of alginate scaffolds. This showed excellent results in cell viability and polymerase chain reaction (PCR) results illustrated gene expression comparable with chondrocytes. The chondrocytes maintained their phenotype and secreted ECM components when in scaffold.³³ This method has a strong level of evidence, is cheap, has great potential, and is optimal for patients under the age of 50 years with chondral lesions 1 cm² to 5 cm² in size³² - Review scores, level of evidence = 2- classification = D

Autologous matrix-induced chondrogenesis. Autologous matrix-induced chondrogenesis (AMIC) uses the microfracture technique. A chondroguide matrix is placed over the surface of the femoral head after microfracture, with the addition of collagens I and III³⁴ to stabilize the blood clot produced.

Autologous matrix-induced chondrogenesis can be performed if the lesion is grade 3 or 4.^{34,35} Fontana et al³⁶ performed a five-year follow-up on AMIC procedures on chondral defects larger than 3 cm². There was a statistically significant improvement in mHHS. This continued up to three years post-operation, with stability observed for the final two years. This showed that AMIC can restore articular cartilage for up to five years or more.

Fontana³⁴ also performed a study comparing AMIC with microfracture and has shown a sustained benefit of AMIC over five years which was better and more durable, compared with microfracture, for lesions larger than 4 cm². From this, we would recommend increasing the level of evidence as this could be a permanent method for restoring articular cartilage in hips. It is estimated that further research would confirm this - Review scores, level of evidence = 2++ classification = B

Table III is our grade system interpretation of the different studies we have discussed. Throughout our scoring and ranking of the different studies, we remained as critical as possible. This, in turn, will highlight any possible room for improvement in future trials.

Discussion

In this review, we have looked at various techniques of cartilage restoration during hip surgery, the results of which are summarized in Tables III and IV. We have uniquely used the GRADE system to compare the studies in various aspects and presented the evidence

Table III. The different studies performed. It shows title, author, age range of patients, follow-up procedure, the surgery performed and the outcome of the surgery

Lead Author	Title	Surgery	Number of Participants	FUP	Age	Outcome
Chen H, (2009) ¹⁰	Drilling and microfracture lead to different bone structure and necrosis during bone-marrow stimulation for cartilage repair.	Microfracture	Animal Models	N/A	N/A	Demonstrated that microfracture can produce long term articular cartilage repair.
Philippon MJ (2008) ¹²	Can microfracture produce repair tissue in acetabular chondral defects?	Microfracture	9	20 mths	N/A	91% was the average fill of lesions after 20 months. However the range was from 25% to 100%.
Byrd JW (2009) ¹⁵	Arthroscopic femoroplasty in the management of cam-type femoroacetabular impingement.	Microfracture	58	16 mths	33	20 point improvement in harris hip scores.
Haviv B (2010) ¹⁶	Arthroscopic femoral osteochondroplasty for cam lesions with isolated acetabular chondral damage.	Microfracture	29	22 mths	37	MHHS score improved by 12, NAHS improved by 13.2
Murakibhavi V (2010) ²⁰	Early results of Autologous Chondrocyte implantation in the hip.	ACI	14	30 mths	N/A	mHHS score improved by 5 points. 5 patients underwent arthroscopy after 1 year. The results showed good integration of new cartilage.
Krych AJ (2011) ²³	Treatment of focal osteochondral defects of the acetabulum with osteochondral allograft transplantation.	Allograft	2	38 mths	28	significant pain improvements, MRI showed plug integration, mHHS scores improved from to 75-97 in 2 years for patient 1 and 79 to 100 in 3 years for patient 2.
Khanna V (2014) ²⁸	Cartilage Restoration of the Hip Using Fresh Osteochondral Allograft: Resurfacing the Potholes.	Allograft	17	42 mths	25.9 (17 to 44)	13/17 had good to fair results (extrapolated from mHHS scores).
Girard J (2011) ²⁹	Osteochondral mosaicplasty of the femoral head.	Mosaicplasty	10	29.2 mths	Above 25	Range of motion increased from 175.4° to 210.7°. Merle d'Aubigné scores improved from 10.5 to 15.5
Field RE (2011) ³⁰	Arthroscopic grafting of chondral defects and subchondral cysts of the acetabulum.	Synthetic osteochondral plug	4	10 mths	N/A	Non-arthritic hip score improved from 53.8 (range 43.8 to 70) pre-operatively to 84.6 (range 78.8 to 87.5) at 6 months.
Mancini D (2014) ³⁵	Five-year results of arthroscopic techniques for the treatment of acetabular chondral lesions in femoroacetabular impingement.	AMIC	31	60 mths	N/A	The mean mHHS improvement at the five year follow-up with respect to preoperative level was 39.1 ± 5.9 on chondral defects larger than 3cm ² .

FUP, follow-up procedure; mHHS, modified Harris Hip Score; NAHS, Non-Arthritic Hip Score; ACI, autologous chondrocyte implantation.

categorization as per GRADE recommendations. We have been able to rank the various techniques using an objective scoring system and have found AMIC to have the greatest success and highest level of evidence. Following a complete review of the literature, the GRADE system was used to produce Table IV.⁶ Regardless of numbers, much more thorough research is demonstrated in the GRADE system.

Our review highlights the relatively poor-quality research available to support these various interventions that have been used. No published randomized controlled trial, which looks at the efficacy of these techniques described to treat chondral defects found in the hip, has yet found its way into the public domain despite the high prevalence of chondral damage noted during hip arthroscopy.

The AMIC procedure appears to have the greatest potential of all current surgical options as it offers a summary of the advantages of the techniques discussed above. It advances the practice of microfracture, increasing the size of lesion treatable beyond 3 cm². The chondroguide matrix with collagen types I and III mimics the

scaffold in synthetic scaffold resurfacing, avoiding the need to acquire stem cells from liposuction. Scaffold resurfacing requires two operations on two different dates, whereas the AMIC is one operation, with the stem cells derived from the blood clot produced by the microfracture. The AMIC procedure surpasses the allograft as it uses self-stem cells. In secondary cases of OA, the causative force should be removed before the AMIC operation. In early-onset cases without obvious causative physiology, we should consider allograft transplant. The patient's genetics may be leading to defective cartilage production, thus the AMIC may only superficially treat OA before the symptoms relapse. Consequently, work on synthetic osteochondral plugs and autografts must be continued. Data from this review have been compiled in Tables III, IV and V. The AMIC procedure is shown as the best technique currently. In Table IV, the studies have been compared by factors such as the patient's number and follow-up procedure. Microfracture has undergone the most research, but it is limited by the type of cartilage regenerate and the size of defects where it could be effective. However, there is very little evidence so far on AMIC,

Table IV. This is a table showing the authors opinions on the grade scoring for the papers discussed in this systematic review

	Microfracture			Mosaicplasty			Synthetic osteochondral plug		Scaffolds	AMIC
Lead Author	Byrd ¹⁵	Philipon ¹²	McDonald ¹⁴	Byrd ¹⁵	Haviv ¹⁶	Krych ²³	Girard ²⁹	Field ³⁰	Kreuz ³²	Fontana ³⁶
Evidence	2	2	2	2	2	2	2	2	2	2
Quality	0	-2	-2	0	-1	-2	-1	-2	-2	-1
Consistency	0	0	-1	0	0	-1	-1	-1	-1	-1
Directness	0	0	-2	0	0	-1	0	-1	-1	0
Effect Size	0	0	0	0	0	0	0	0	0	0
Total	2	0	-3	2	1	-2	0	-2	-2	0

AMIC, autologous chondrocyte implantation.

Table V. The different techniques compared by authors opinion (8 ranks as the best and 1 as worst)

	Microfracture	Autograft	Allograft	Mosaicplasty	Synthetic osteochondral plug	Synthetic scaffold resurfacing	AMIC
Lesion size	4 cm ²	5-6 cm ²	15 cm ²	5 cm ²	2 cm ²	5 cm ²	5 cm ²
Subchondral layer damage in surgery	Yes	Intact or breached	Intact or breached	Intact or breached	Intact or breached	Intact	Yes
Number of surgeries	1	2	1	1	1	2	1
Donor morbidity	N/A	Minimal	None	N/A	None	None	N/A
Risk of disease transmission	None	None	Low	None	Very low	None	N/A
Recovery time post-surgery	Three mths to return to sport	Four mths return to sport	Four mths return to sport	Two wks bed rest	Four mths return to sport	Six to 12 mths	Six mths
Ranking against other techniques (8 = best)	6	4	4	5	2	1	7

AMIC, autologous matrix-induced chondrogenesis.

and therefore we should not get too carried away with the potential of this technique. There should now be a drive to build up a strong case for the use of AMIC in the restoration of articular cartilage in the hip.

In conclusion, there is little long-term research into cartilage regeneration in the hip. Greater focus on manipulating the techniques used in the knee is needed, as is a drive into the earlier, pre-symptomatic diagnosis of OA. Earlier detection of chondral lesions would enable use of the current techniques to prevent the latter stages of the disease, avoiding the only current surgical option, THA. The AMIC procedure currently seems to have the strongest evidence base, but higher-powered randomized controlled trials are required.

Supplementary material



The study's PRISMA flow diagram

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Author Contributions

- W. E. Hotham: Primary author, Carried out the analysis, acquired the data, and wrote the paper.
- A. Malviya: Supervisor of the study and acted as a preliminary editor.

Conflict of Interest Statement

- None declared

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