Journal of Cartilage & Joint Preservation® 2 (2022) 100053

Contents lists available at ScienceDirect

Journal of Cartilage & Joint Preservation®

journal homepage: www.elsevier.com/locate/jcjp

Moving towards single stage cartilage repair—is there evidence for the minced cartilage procedure?

Armin Runer[a,*], and Gian M. Salzmann[b,c]

[a] Department for Orthopaedic Sports Medicine, Technical University Munich, Munich, Germany
[b] Gelenkzentrum Rhein-Main, Wiesbaden, Germany
[c] Lower Extremity Orthopaedics, Musculoskeletal Centre, Schulthess Clinic, Zurich, Switzerland

ARTICLE INFO

Keywords:
Minced cartilage
Autologous cartilage
Particulated cartilage
Cartilage chips
Cartilage defect
Chondral defect

ABSTRACT

Introduction: Several different surgical options are available to address cartilage lesions. Lately, autologous minced cartilage procedure has been gaining in popularity as a chondrocyte based, simple, single-staged and cost-effective surgical technique.

Objective: The aim of this review is to provide an overview of the current evidence supporting chondrocyte based, single-stage cartilage repair with a focus on the technique of autologous minced cartilage implantation.

Results: To date only limited evidence exists for single staged, autologous minced cartilage procedure. *In vitro* and animal studies show induction of *de novo* production of extracellular matrix, chondrocyte outgrowth, proliferation, and differentiation with encouraging tissue generation. Biological, histological and immunohistological data seem comparable to 2-stage autologous chondrocyte implantation. Preliminary, short-term clinical data indicate good clinical and functional results with low complication and revision rates. Clinical outcomes in the short term seem comparable to those resulting from autologous chondrocyte implantation .

Conclusion: Single-stage autologous minced cartilage repair is a simple and effective cartilage repair option. This technique has strong biologic, economic and clinical potential. More high-level, long-term comparative trials with larger patient cohorts are needed to allow for comparison with other cartilage repair techniques and to determine the implant durability.

Introduction

There is an increasing incidence of chondral and osteochondral lesions. Knee cartilage defects are reported to be as high as 36% in athletes.[1] Untreated lesions cause higher stress concentration around the rim of the defect,[2–4] changes in the subchondral bone[5] and changes in the intraarticular joint homeostasis due to an elevation of intra-articular inflammatory cytokine concentration[6] and may therefore lead to early onset arthritis. This not only places a higher burden to the patient but also creates additional costs in the healthcare system. Therefore, appropriate cartilage repair techniques are needed, with the aim to maximize the amount of mature and organized hyaline or hyalinelike cartilage to reduce pain, maximize function and prevent future joint degeneration.

Several surgical options are available to address focal cartilage lesions, including bone marrow stimulation techniques (ie, microfractures), osteochondral auto- or allograft transplantation and autologous chondrocyte implantation (ACI).[7–9,1,10] Each of these surgical options has advantages and disadvantages which make the treatment of cartilage lesions challenging. Local treatment guide-

* Gian Salzmann, Lower Extremity Orthopaedics, Musculoskeletal Centre, Schulthess Clinic, Lengghalde 2, 8008 Zürich, Switzerland.
Email address: armin.runer@tum.de (A. Runer).

https://doi.org/10.1016/j.jcjp.2022.100053
Received 22 March 2022; Revised 15 April 2022; Accepted 28 April 2022
Available online 4 May 2022
2667-2545/© 2022 The Author(s). Published by Elsevier B.V. on behalf of International Cartilage Regeneration and Joint Preservation Society. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

lines exist.[11,12] Yet, these often have overlapping indications and remain a constant matter of debate. Especially in patients with large diameter defects, osteochondral lesions or in revision cases strong evidence for the optimal treatment strategy is missing.

Bone marrow stimulation techniques, such as microfracturing or subchondral drilling, are cheap and fast but limited to small chondral lesions.[13,14] Early postoperative results are promising and comparable to alternative techniques, however mid- to long-term results deteriorate, possibly due to inferior biochemical and biomechanical characteristics of the formed regenerative tissue.[15,14] Nowadays, ACI is considered to be the first line therapy for medium to large defects because it can result in hyaline- or hyaline-like cartilage and favorable clinical outcomes.[16,13,17,18,14] However, disadvantages of ACI are high laboratory cell expansion costs, possible altered cell quality at time of implantation (dedifferentiation and senescence) and a 2-stage surgical approach being required.[7,9,19]

In order to overcome these drawbacks, single-staged procedures, such as particulated autologous or allogenic cartilage have been developed and introduced. The principal concept has been described initially by Albrecht et al in the early 1980s[20,21] and was picked up again emphatically by Lu et al in 2006.[22] Recently, minced cartilage has gained in interest especially due to several advantages, such as being a simple, single stage procedure that can be performed in an arthroscopic or mini-arthrotomy surgical approach and may offer strong biologic potential..[23,19]

The following review presents available biologic, *in vitro, in vivo*, and clinical evidence for single-stage autologous cartilage repair with particular emphasis on the minced cartilage procedure.

Biologic background

Damaged articular cartilage induces an inflammatory response within the joint by a complex interplay of genetic, metabolic, biochemical, and biomechanical factors which results in a limited capacity for regeneration and self-repair.[24,25] Chondrocyte proliferation and dedifferentiation, a process where chondrocytes lose their feature of high differentiation resulting in a changed phenotype with less collagen II content, is a pathologic process within damaged cartilage tissue. As a consequence, biomechanically inferior connective tissue (fibrocartilage) is produced.[19] This process has also been demonstrated to take place in tissue engineering laboratories *in vitro*, and it remains unclear whether such cells are capable of redifferentiation when implanted *in vivo*.[26,19,27] Contrary, chondrocytes which are embedded in their native, *in vivo* environment may have the potential to proliferate physiologically without dedifferentiation and can maintain therefore their native characteristics,[1928] In addition, recent findings have highlighted the important role of mechanical stimuli in promoting proliferation and chondrogenic differentiation.[29,30]

This biochemical and biomechanical *in vivo* environment within the joint, which is hardly reproducible *in vitro* due to its complexity, could be one major advantage with regard to the biologic potential of the minced cartilage procedure. Slicing healthy cartilage into small pieces has shown to “activate” chondrocytes and have a physiologic response to encourage chondrogenic proliferation, increased extra cellular matrix (ECM) production, and fill the cartilage defects.[19] Furthermore, outgrowth of activated chondrocytes is promoted by increasing the surface area of the tissue.[31,22,19] This results in proliferation, differentiation and finally restoration of hyaline or hyaline-like cartilage.[22,19,32] Particle size positively correlates with *in vitro* production of ECM, suggesting that an increased fragmentation upregulates ECM production.[23] On the other hand, cartilage outgrowth seems limited when the harvested cartilage is not particulated and, therefore, activated.[33] Currently cartilage mincing may be performed by using a knife, specially designed mincing devices, or arthroscopic shaver devices.[34,31,19]

Cartilage harvesting can be performed from the delaminated boarder of the cartilage defect or from low weight-bearing areas of the joint. Aurich et al[35] reported that redifferentiating lesion-associated chondrocytes resulted in greater chondrogenic potential compared to expanded dedifferentiated chondrocytes. Furthermore, superior redifferentiation potential of cartilage harvested close to the defect margin (cartilage lesion associated chondrocytes) was observed.[35] Similar results are reported *in vitro* studies showing topographical cartilage variations with clear differences regarding gene and matrix expression profiles between nonweightbearing and weight-bearing cartilage, favoring the latter one.[36]

Moving towards 1-stage

In vitro evidence and animal studies

Already in 1983 Albrecht et al[20] treated osteochondral defects of rabbits with single-stage autologous cartilage fragments and a special fibrin adhesive. The results were compared to a control group who did not receive any treatment. In the cartilage fragmentation group, complete closure of defects by hyaline or hyaline-like cartilage was achieved while no hyaline cartilage was histologically observed in the control group.

In 2006, Lu et al[22] cultured human minced cartilage tissue *in vitro* under standard chondrogenic culturing conditions. Cell outgrowth and interconnection with newly deposited extracellular matrix was revealed after 6 weeks. Moreover, an inverse relationship between outgrowth efficiency and tissue fragment size was detected, a fact, that was later also confirmed by Bonasia et al.[23] When implanted in mice, cartilage-like tissue was formed by chondrocytes outgrown into 3-D scaffolds while neither matrix deposition nor comparable cell morphology and cellularity was produced in scaffold alone controls. Moreover, the therapeutic use of minced cartilage and resorbable scaffold in goats for full-thickness chondral defects produced hyaline-like repair tissue at 6 months.

In 2008, Lind et al[37] studied cartilage repair response in a goat model comparing autologous cartilage chips and cultured autologous chondrocytes (ACI) in combination with a collagen membrane. No significant microscopic, mechanical, or histological differences were reported between both treatment options after 4 months.

In 2009, Frisbie et al[38] compared four different treatment options for chondral defects in a *in vivo* horse model: (1) no treatment with empty defect, (2) fragmented cartilage on a scaffold (cartilage autograft implantation system [CAIS]), (3) empty scaffold and (4) ACI. Superior results in arthroscopic, histologic, and immunohistochemistry parameters were found for CAIS and ACI compared with control groups, whereas similar outcomes were seen between CAIS and ACI. Best microscopic scores were observed in the CAIS group.

In 2012 and 2013 Marmotti et al[39,40] reported in 2 *in vitro* studies a time-dependent chondrocyte outgrowth with high cellularity and positive collagen type II immunostaining after seeding cartilage fragments from rabbit- or goat onto 3D scaffolds. Subsequently, the same membrane scaffolds were used in an *in vivo* rabbit model, showing that autologous cartilage fragment-loaded scaffolds induced significantly better repair tissue than the scaffold alone.[39] When used in goats, autologous cartilage fragments loaded onto scaffold composed of a hyaluronic acid-derived membrane, platelet-rich fibrin matrix and fibrin glue produced significant functional hyaline-like repair tissue with superior histological and mechanical characteristics compared to scaffold alone or untreated.[40]

Wang et al[30] in 2014, tested different *in vitro* culture conditions (free swelling vs dynamic compression and shear forces) on general chondrogenesis of minced cartilage fragments revealing a successful outgrowth and neomatrix formation in all groups. Histology and immunohistochemistry analysis showed that stronger cellular outgrowth but weaker collagen type II and aggrecan expression was detected under loading conditions.

Tsuyuguchi et al[29] compared the benefits of minced cartilage, obtained from patients with knee osteoarthritis, over isolated chondrocytes in atelocollagen gel on cell migration, proliferation, and matrix production. Histologically, the minced cartilage group showed cell migration from fragments into the gel, with the Bern score and cell count being significantly higher than those in the control group. Moreover, cell migration, proliferation, and glycosaminoglycan content were superior in the minced cartilage group.

Contrary to the above-mentioned findings, Andjelkov et al[41] reported no outgrowth of cultured human arthritic chondrocytes into a fibrin matrix after 2 to 5 weeks.

Christensen et al[42] in 2016, treated osteochondral knee lesions in minipigs with either autologous bone and minced cartilage chips (autologous dual-tissue transplantation [ADTT]) or with autologous bone graft alone. Treatment with autologous bone and cartilage chips resulted in a significant higher fraction of hyaline tissue and fibrocartilage at 6 and 12 months postoperative, whereas the fraction of fibrous tissue was lower compared with autologous bone alone. After 12 month the fraction of hyaline tissue has significantly decreased in the autologous bone graft group (4.8%) whereas it remained unchanged in the ADTT group (20.1%). The authors concluded that the presence of minced cartilage chips facilitated the formation of fibrocartilage as opposed to fibrous tissue in osteochondral defects in minipig knees and that the implanted cartilage chips remain viable even after 12 months.

In a similar study setup, Christensen et al[43] investigated the *in vivo* cartilage repair outcome of autologous cartilage chips compared with bone marrow stimulation (microfracture) in full-thickness cartilage defects in a minipig model. Again, improved quality of cartilage repair tissue with significant more hyaline cartilage 17.1%), collagen type II staining (54.5%) but less fibrous tissue (23.8%) was found in the ACC group compared to the MFX group (2.9%, 28.1%, and 41.1%, respectively).

Perez et al[44] investigated in a sheep model the chondrogenic-regenerative properties of hyaline cartilage chips combined with a growth factors-based clot and an intraarticular PRP injection for full-thickness defects. After 6 month, nearly normal macroscopical and microscopical tissue appearance was observed. Histological analysis of the neocartilage revealed equivalent structure to mature cartilage tissue and a collagen expression pattern in the newly formed cartilage like that found in surrounding healthy articular cartilage.

Olsen et al[45] compared autologous fragmented cartilage in chondral defects of mini pigs with and without addition of PRP and found no significant difference between both groups with approximately 20% hyaline cartilage, 50% fibrocartilage, and 22% fibrous tissue.

Matsushita et al[46] performed an *in vitro* study examining the ability of chondrocyte migration and proliferation from minced cartilage in atelocollagen gel reporting a significant increase in the number of chondrocytes and abundant matrix in the minced cartilage group compared to the ACI group. In an *in vivo* rabbit model, trochlea defects were created, and 4 different treatment groups build: (1) defect left empty, (2) Filled with allogenic minced cartilage, (3) filled with isolated allogenic chondrocytes embedded in atelocollagen gel (ACI group) and (4) filled with atelocollagen gel and a periosteal flap. After 24 months, minced cartilage and ACI had superior results compared to group 1 and group 4. Histological and immunohistochemistry revealed no significant difference between minced cartilage and ACI. The authors concluded that implantation of minced cartilage embedded in atelocollagen gel showed good cartilage repair equivalent to ACI.

In 2019, Ao et al[47] compared particulated juvenile allograft cartilage (PJAC) to autologous (adult) cartilage chips (ACC) in 30 minipigs after 1, 3, and 6 months. While significantly more hyaline cartilage was found in the ACC group compared to PJAC after one month (29.4% vs 20.1%), and significantly more fibrocartilage content after 1 and 3 months 27.4% vs 18.2% and 49.9% vs 41.1%, respectively), no differences were observed at final follow up. Fibrous tissue was higher in the PJAC group. Similar, higher semiquantitative scores and higher rates of immunohistochemical staining were found in the ACC group compared with PJAC at 1 and 3 months, but not at 6 months.

Summarizing *in vitro* and animal studies, fragmenting autologous cartilage induces *de novo* production of extra cellular matrix, chondrocyte outgrowth, proliferation, and differentiation. This process is enhanced by using 3D scaffolds as well as mechanical and biological stimuli. Furthermore, these data demonstrate, that from a biological, histological and immunohistological point of view, 1-step cartilage repair seems feasible and comparable to ACI.

Surgical technique

Preoperative planning and surgical technique for minced cartilage procedure have been described previously in detail.[48,49,10] In summary, preoperative planning is mandatory and includes magnetic resonance imaging (MRI) and conventional radiographs.[49] It is of utmost importance, to address coexisting pathologies, especially ligamentous instabilities, meniscus deficiencies and mechanical axis malalignments prior to cartilage repair. The final decision on chondral repair is made only after detailed arthroscopic examination of the defect. Subsequently, cartilage harvesting can be performed either via osteochondral cylinders from low weight bearing knee areas (eg, intercondylar notch) or using alternative harvesting methods like special scrapes and arthroscopic shavers with tissue collector.[49,10] When using osteochondral cylinders, the cartilage must be separated from the bone and then fragmented with a blade until a paste like appearance is obtained. Fragmentation is not needed when using arthroscopic shavers. Following standard defect preparation with creation of vertical cartilage walls, the calcified layer may be removed, the joint is aspirated to create a dry-scope environment, and the minced cartilage paste is implanted to the defect. Autologous thrombin and platelet rich plasma (PRP), fibrin glue or a membrane may be used to obtain a stable fixation depending on the technique[50,46,49,19,10]

Clinical data

When looking into single-staged cartilage repair technique, 4 different methods were described for clinical use[51]: (1) the CAIS is a minced autologous cartilage embedded in a synthetic scaffold system; (2) PJAC allograft technique; (3) autologous minced cartilage—with and without concomitant bone grafting and (4) augmented autologous minced cartilage.

As far as the authors are aware, there is only 1 clinical study for CAIS[52] and 3 trials for autologous minced cartilage.[53,54,50]

The first clinical trial with autologous fragmented cartilage was performed in 2011 by Cole et al,[52] who evaluated the safety and outcomes of CAIS. Twenty-nine patients were randomized to either microfracture ($n = 9$) or CAIS ($n = 20$) and followed for 2 years. Patient reported outcome measurements indicated an overall improvement in both groups. The International Knee Documentation Committee- (IKDC-) and Knee Injury and Osteoarthritis Outcome Score (KOOS) score were significantly high in the CAIS- compared to the microfracture group at final follow up. MRI data revealed that patients treated with microfracturing had significantly higher incidence of intralesional osteophyte formation. No group differences were observed in fill of the graft bed, tissue integration, or presence of subchondral cysts. A larger randomized controlled trial has been withdrawn by the company in 2013. CAIS is currently not available for patients.

In 2015, Christensen et al[53] treated 8 patients suffering from osteochondrosis dissecans in the knee with a combination of autologous bone graft and autologous cartilage chips embedded in fibrin glue (ADTT). One year postoperative, it was observed that the magnetic resonance observation of cartilage repair tissue (MOCART) score improved significantly from 22.5 to 52.5. Computed tomography imaging demonstrated very good subchondral healing with over >80% bone filling. Patient reported outcome measurements improved significantly. Treatment of osteochondrosis dissecans with ADTT resulted in very good subchondral bone restoration and good cartilage repair.

In 2019, Massen et al[50] followed 27 consecutive patients treated with second-generation minced cartilage implantation technique due to chondral or osteochondral lesions for 2 years. At final follow-up, there was a significant decrease in pain from 7.2 ± 1.9 to 1.8 ± 1.6 and a significant increase in knee function from 7.2 ± 2.0 to 2.1 ± 2.3 on the numeric analog scale. Furthermore, significant radiological improvements were observed in the MOCART score at final follow up. The authors concluded that patients undergoing single-step autologous minced cartilage procedure reported satisfactory outcomes at 2-year follow-up. Autologous minced cartilage procedure does represent a possible alternative to standard autologous chondrocyte implantation.

In 2020, Cugat et al[54] embedded autologous cartilage chips in a clot with plasma poor in platelets (PPP) and PRP to treat 15 patients with full-thickness cartilage or osteochondral defects. After 15 months of follow-up statistically significant improvement between pre- and postoperative periods for visual analogue scale for pain, Lysholm score, IKDC subjective form, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain, WOMAC for stiffness, WOMAC for function, Lequesne Index and the Short-Form 12 physical component summary was observed. In addition, a significant improvement in the MOCART score was observed. The authors concluded that a single-stage chondral repair with hyalin cartilage chips embedded in PPP and PRP provides excellent clinical, functional, and MRI-based outcomes in young, active individuals with full-thickness cartilage or osteochondral defects.

While all the above-mentioned clinical studies were performed in the knee joint, autologous minced cartilage implantation has more recently been applied to other joints (hip, shoulder, ankle) to treat chondral or osteochondral defects.[55,56,48,57]

In summary, there remains limited clinical outcomes of autologous minced cartilage procedures to-date, but new techniques for graft recovery, fragmentation, graft delivery and fixation continue to evolve. The available data show good clinical and functional results with low complication and revision rates comparable to other available cartilage repair techniques. More high- level comparative trials as well as mid- to long-term outcomes are needed.

In countries where chondral allografts are widely available, particulated juvenile allograft cartilage technique might be an alternative to minced cartilage. This technique can be used especially when delaminated cartilage from the defect margin is not available and the harvesting of cartilage from healing areas of the joint is to be avoided. Reports on immature chondrocytes show an increased proliferative activity, cell density, and metabolic activity when compared to adult chondrocytes.[58–61] Short term results have shown good and promising results for treatment of patella, trochlea or femoral condyle defects in terms of pain, function as well as defect filling and histological outcomes.[62–64] Positive patient-reported long-term outcomes are also reported for a cohort of patients with difficult osteochondral lesions of the talus.[65]

Table 1
Comparison of outcome measurements of matrix associated autologous chondrocyte implantation (MACI) and autologous minced cartilage for cartilage lesions in the knee.

Outcome measurement	Matrix associated autologous chondrocyte implantation (MACI)*	Autologous minced cartilage
IKDC score	65-70[67–69]	57-81[53,52,54]
KOOS score (24 mo postoperative)	Pain: 82-86[67,70,68,71] ADL: 83-88[67,70,68,71] QOL: 55-83[70,67,68,71]	Pain: 91[52] ADL: 97[52] QOL: 69[52]
MOCART Score	63-82[12,72,71,69]	47-70[53,54,50]

Abbreviations: ADL, activities of daily living; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; MOCART, magnetic resonance observation of cartilage repair tissue; QOL, quality of life.

* Only randomized controlled trials with a 2 year follow-up are included in this table.

Single-stage vs 2-stage cartilage repair

Matrix induced Autologous chondrocyte implantation (MACI) represents today the gold standard for moderate to large cartilage defects..[12] Several studies have shown a clear superiority in structural outcomes of ACI over therapies based on bone marrow stimulation techniques alone.[12,66]

While no clinical studies have directly compared autologous minced cartilage procedure to ACI, standardized patient reported outcome measurements and MRI forms can be compared between the individual studies.

Below, outcomes for standardized and widely used questionnaires and evaluation forms are summarized for ACI/MACI and autologous minced cartilage procedure

International knee documentation committee (IKDC) score

Reported IKDC subjective score for MACI in RCTs ranged from 65 to 70 after 2 years.[67–69] Cole et al[52] reported for CAIS an IKDC score of 59 ± 13 after 24 months. Comparable results for minced cartilage were also shown by Christensen et al[53] with a IKDC value of 68 ± 15 while a higher score of 81 ± 17 was reported by Cugat et al.[54]

Knee injury and osteoarthritis outcome score (KOOS)

For MACI four RCTs[67,70,68,71] reported 24 months values of KOOS subscales for pain, activities of daily living (ADL) and knee-related quality of life (QOL). Homogeneous results with values between 82 and 86 for pain, 83 and 88 for ADL, and 55 and 83 for QOL were reported. For minced cartilage procedures, only Cole et al[52] reported 24 months outcomes for KOOS subscales being 91 ± 8 (pain), 97 ± 4 (ADL) and 69 ± 23 (QOL).

MOCART score

For MACI procedures, MOCART scores were reported in three RCTs[12,72,69] ranging between 63 and 82 after 12 months whereas for autologous cartilage particulate procedures, the score ranged between 47 and 70.[53,54,50]

In summary, the limited amount of available data as well as the inhomogeneous patients groups especially for cartilage particulate procedures does not allow for a direct comparison between both procedures. However, both patient reported outcome measurements and postoperative MRI data appear similar between both cartilage restoration procedures (Table 1). Table 2 represents pros and cons of chondrocyte-based cartilage repair techniques.

Outlook using single-stage cartilage repair procedures

Preliminary, clinical and functional data show encouraging and promising results, however there are still several aspects that need to be addressed and clarified.

Arthroscopic techniques for minced cartilage implantation have been well described. While recent advancements have been made available to market, further development and refinement may continue to aid reproducibility, ease and time of procedure.

The optimal fixation technique for autologous cartilage particulate offers another avenue for consideration. Currently, several options including staples, a membrane, fibrin glue, and membrane-fibrin glue combination for open procedures or hydrogel, PPP/PRP or autologous thrombin for arthroscopic techniques are available.[19]

Further studies are necessary, to specify the optimal defect size for the minced cartilage procedure. It would be worth considering that the single-stage minced cartilage procedure could also be used to treat smaller cartilage defects that have previously been treated with bone marrow stimulation techniques.[19]

Table 2
Characteristics of chondrocyte-based cartilage repair techniques.

Method	Pros	Cons
Autologous chondrocyte implantation (ACI/MACI)	- Autologous cells/tissue - Available long-term outcomes - Strict regulations and quality assessments - Different application techniques - No violation of subchondral bone - Small to large defects - Hyalin-like cartilage - Good postoperative short and long-term results	- Two stage surgery - Higher costs - worse outcomes in patients with prior bone stimulation[73]
Particulated juvenile articular cartilage (PJAC)	- Single stage surgery - Moderate costs - Off-the-shelf - Juvenil cells - Small to large defects - Hyalin-like cartilage - Good postoperative short-term results	- No long-term data - Limited high-level evidence - Availability of donor tissue - Possible national regulatory with human donors - Allograft tissue - Unknown outcomes in patients with prior bone stimulation - Lower and upper defect size limits have yet to be defined
Autologous minced cartilage with or without augmentation	- Single stage surgery - Relative low cost - Autologous tissue - No violation of subchondral bone - Small to large defects - Hyalin-like cartilage - Open and arthroscopical technique - Good postoperative short-term results	- No long-term data - Limited high-level evidence - Optimal fixation technique has yet to be defined - Lower and upper defect size limits have yet to be defined - unknown outcomes in patients with prior bone stimulation

Finally, high-level, mid- to long-term follow-up, comparative studies with large patient cohorts including clinical, functional, and radiological data are needed to allow for comparison with other cartilage repair techniques and to determine the implant durability.

Conclusion

Based on the available *in vitro* and *in vivo* data, autologous minced cartilage repair is a promising single-stage cartilage repair procedure with strong biologic, economic and clinical potential. Further high-level, long-term, comparative clinical trials with larger cohorts are necessary to allow for comparison with other cartilage repair techniques and to determine the implant durability.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Salzmann G is a consultant for Arthrex.

Authorship contributions

AR: draft of the manuscript. GS: draft of the manuscript and critical revision.

Patient informed consent

For this review article, there is no Patient Informed Consent Statement required.

References

1. Flanigan DC, Harris JD, Trinh TQ, Siston RA, Brophy RH. Prevalence of chondral defects in athletes' knees: a systematic review. *Med Sci Sports Exerc*. 2010;42:1795–1801.
2. Coetzee JC, Giza E, Schon LC, et al. Treatment of osteochondral lesions of the talus with particulated juvenile cartilage. *Foot Ankle Int*. 2013;34:1205–1211.
3. Gratz KR, Wong BL, Bae WC, Sah RL. The effects of focal articular defects on cartilage contact mechanics. *J Orthop Res*. 2009;27:584–592.

4. Guettler JH, Demetropoulos CK, Yang KH, Jurist KA. Osteochondral defects in the human knee: influence of defect size on cartilage rim stress and load redistribution to surrounding cartilage. *Am J Sports Med*. 2004;32:1451–1458.
5. Minas T, Nehrer S. Current concepts in the treatment of articular cartilage defects. *Orthopedics*. 1997;20:525–538.
6. Fraser A, Fearon U, Billinghurst RC, et al. Turnover of type II collagen and aggrecan in cartilage matrix at the onset of inflammatory arthritis in humans: relationship to mediators of systemic and local inflammation. *Arthritis Rheum*. 2003;48:3085–3095.
7. Bonasia DE, Marmotti A, Rosso F, Collo G, Rossi R. Use of chondral fragments for one stage cartilage repair: a systematic review. *World J Orthop*. 2015;6:1006–1011.
8. Dekker TJ, Aman ZS, DePhillipo NN, Dickens JF, Anz AW, LaPrade RF. Chondral lesions of the knee: an evidence-based approach. *J Bone Joint Surg Am*. 2021;103:629–645.
9. Evenbratt H, Andreasson L, Bicknell V, Brittberg M, Mobini R, Simonsson S. Insights into the present and future of cartilage regeneration and joint repair. *Cell Regen*. 2022;11:3.
10. Schneider S, Ossendorff R, Holz J, Salzmann GM. Arthroscopic minced cartilage implantation (MCI): a technical note. *Arthrosc Tech*. 2021;10:e97–e101.
11. Filardo G, Andriolo L, Angele P, et al. Scaffolds for knee chondral and osteochondral defects: indications for different clinical scenarios. *A Consensus Statement. Cartilage*. 2021;13:1036S–1046S.
12. Niemeyer P, Albrecht D, Andereya S, et al. Autologous chondrocyte implantation (ACI) for cartilage defects of the knee: a guideline by the working group "Clinical Tissue Regeneration" of the German Society of Orthopaedics and Trauma (DGOU). *Knee*. 2016;23:426–435.
13. Chimutengwende-Gordon M, Donaldson J, Bentley G. Current solutions for the treatment of chronic articular cartilage defects in the knee. *EFORT Open Rev*. 2020;5:156–163.
14. Riboh JC, Cvetanovich GL, Cole BJ, Yanke AB. Comparative efficacy of cartilage repair procedures in the knee: a network meta-analysis. *Knee Surg Sports Traumatol Arthrosc*. 2017;25:3786–3799.
15. Gill TJ, Asnis PD, Berkson EM. The treatment of articular cartilage defects using the microfracture technique. *J Orthop Sports Phys Ther*. 2006;36:728–738.
16. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med*. 1994;331:889–895.
17. Gikas PD, Bayliss L, Bentley G, Briggs TW. An overview of autologous chondrocyte implantation. *J Bone Joint Surg Br*. 2009;91:997–1006.
18. Grevenstein D, Mamilos A, Schmitt VH, et al. Excellent histological results in terms of articular cartilage regeneration after spheroid-based autologous chondrocyte implantation (ACI). *Knee Surg Sports Traumatol Arthrosc*. 2021;29:417–421.
19. Salzmann GM, Ossendorff R, Gilat R, Cole BJ. Autologous minced cartilage implantation for treatment of chondral and osteochondral lesions in the knee joint: an overview. *Cartilage*. 2021;13:1124s–1136s.
20. Albrecht F, Roessner A, Zimmermann E. Closure of osteochondral lesions using chondral fragments and fibrin adhesive. *Arch Orthop Trauma Surg*. 1983;101:213–217.
21. Albrecht FH. [Closure of joint cartilage defects using cartilage fragments and fibrin glue]. *Fortschr Med*. 1983;101:1650–1652.
22. Lu Y, Dhanaraj S, Wang Z, et al. Minced cartilage without cell culture serves as an effective intraoperative cell source for cartilage repair. *J Orthop Res*. 2006;24:1261–1270.
23. Bonasia DE, Marmotti A, Mattia S, et al. The degree of chondral fragmentation affects extracellular matrix production in cartilage autograft implantation: an *in vitro* study. *Arthroscopy*. 2015;31:2335–2341.
24. Buckwalter JA. Articular cartilage injuries. *Clin Orthop Relat Res*. 2002. doi:10.1097/00003086-200209000-0000421-37.
25. Haseeb A, Haqqi TM. Immunopathogenesis of osteoarthritis. *Clin Immunol*. 2013;146:185–196.
26. Darling EM, Athanasiou KA. Rapid phenotypic changes in passaged articular chondrocyte subpopulations. *J Orthop Res*. 2005;23:425–432.
27. Zhao Z, Fan C, Chen F, et al. Progress in articular cartilage tissue engineering: a review on therapeutic cells and macromolecular scaffolds. *Macromol Biosci*. 2020;20:e1900278.
28. Barry F, Murphy M. Mesenchymal stem cells in joint disease and repair. *Nat Rev Rheumatol*. 2013;9:584–594.
29. Tsuyuguchi Y, Nakasa T, Ishikawa M, et al. The benefit of minced cartilage over isolated chondrocytes in atelocollagen gel on chondrocyte proliferation and migration. *Cartilage*. 2021;12:93–101.
30. Wang N, Grad S, Stoddart MJ, et al. Particulate cartilage under bioreactor-induced compression and shear. *Int Orthop*. 2014;38:1105–1111.
31. Levinson C, Cavalli E, Sindi DM, et al. Chondrocytes from device-minced articular cartilage show potent outgrowth into fibrin and collagen hydrogels. *Orthop J Sports Med*. 2019;7:2325967119867618.
32. Tseng TH, Jiang CC, Lan HH, Chen CN, Chiang H. The five-year outcome of a clinical feasibility study using a biphasic construct with minced autologous cartilage to repair osteochondral defects in the knee. *Int Orthop*. 2020;44:1745–1754.
33. Zingler C, Carl HD, Swoboda B, Krinner S, Hennig F, Gelse K. Limited evidence of chondrocyte outgrowth from adult human articular cartilage. *Osteoarthritis Cartilage*. 2016;24:124–128.
34. Hunziker EB, Quinn TM, Hauselmann HJ. Quantitative structural organization of normal adult human articular cartilage. *Osteoarthritis Cartilage*. 2002;10:564–572.
35. Aurich M, Hofmann GO, Best N, Rolauffs B. Induced redifferentiation of human chondrocytes from articular cartilage lesion in alginate bead culture after monolayer dedifferentiation: an alternative cell source for cell-based therapies? *Tissue Eng Part A*. 2018;24:275–286.
36. Salzmann GM, Buchberger MS, Stoddart MJ, et al. Varying regional topology within knee articular chondrocytes under simulated in vivo conditions. *Tissue Eng Part A*. 2011;17:451–461.
37. Lind M, Larsen A. Equal cartilage repair response between autologous chondrocytes in a collagen scaffold and minced cartilage under a collagen scaffold: an *in vivo* study in goats. *Connect Tissue Res*. 2008;49:437–442.
38. Frisbie DD, Lu Y, Kawcak CE, DiCarlo EF, Binette F, McIlwraith CW. In vivo evaluation of autologous cartilage fragment-loaded scaffolds implanted into equine articular defects and compared with autologous chondrocyte implantation. *Am J Sports Med*. 2009;37(Suppl 1):71S–80S.
39. Marmotti A, Bruzzone M, Bonasia DE, et al. One-step osteochondral repair with cartilage fragments in a composite scaffold. *Knee Surg Sports Traumatol Arthrosc*. 2012;20:2590–2601.
40. Marmotti A, Bruzzone M, Bonasia DE, et al. Autologous cartilage fragments in a composite scaffold for one stage osteochondral repair in a goat model. *Eur Cell Mater*. 2013;26:15–31 discussion 31-12.
41. Andjelkov N, Hamberg H, Bjellerup P. No outgrowth of chondrocytes from non-digested particulated articular cartilage embedded in commercially available fibrin matrix: an *in vitro* study. *J Orthop Surg Res*. 2016;11:23.
42. Christensen BB, Foldager CB, Olesen ML, Hede KC, Lind M. Implantation of autologous cartilage chips improves cartilage repair tissue quality in osteochondral defects: a study in gottingen minipigs. *Am J Sports Med*. 2016;44:1597–1604.
43. Christensen BB, Olesen ML, Lind M, Foldager CB. Autologous cartilage chip transplantation improves repair tissue composition compared with marrow stimulation. *Am J Sports Med*. 2017;45:1490–1496.
44. Dominguez Perez JM, Fernandez-Sarmiento JA, Aguilar Garcia D, et al. Cartilage regeneration using a novel autologous growth factors-based matrix for full-thickness defects in sheep. *Knee Surg Sports Traumatol Arthrosc*. 2019;27:950–961.
45. Olesen ML, Christensen BB, Foldager CB, Hede KC, Jorgensen NL, Lind M. No effect of platelet-rich plasma injections as an adjuvant to autologous cartilage chips implantation for the treatment of chondral defects. *Cartilage*. 2021;13:277S–284S.
46. Matsushita R, Nakasa T, Ishikawa M, et al. Repair of an osteochondral defect with minced cartilage embedded in atelocollagen gel: a rabbit model. *Am J Sports Med*. 2019;47:2216–2224.
47. Ao Y, Li Z, You Q, Zhang C, Yang L, Duan X. The use of particulated juvenile allograft cartilage for the repair of porcine articular cartilage defects. *Am J Sports Med*. 2019;47:2308–2315.
48. Roth KE, Ossendorff R, Klos K, Simons P, Drees P, Salzmann GM. Arthroscopic minced cartilage implantation for chondral lesions at the talus: a technical note. *Arthrosc Tech*. 2021;10:e1149–e1154.
49. Salzmann GM, Calek AK, Preiss S. Second-generation autologous minced cartilage repair technique. *Arthrosc Tech*. 2017;6:e127–e131.

50. Massen FK, Inauen CR, Harder LP, Runer A, Preiss S, Salzmann GM. One-step autologous minced cartilage procedure for the treatment of knee joint chondral and osteochondral lesions: a series of 27 patients with 2-year follow-up. *Orthop J Sports Med*. 2019;7:2325967119853773.
51. Christensen BB, Olesen ML, Hede KTC, Bergholt NL, Foldager CB, Lind M. Particulated cartilage for chondral and osteochondral repair: a review. *Cartilage*. 2021;13:1047S–1057S.
52. Cole BJ, Farr J, Winalski CS, et al. Outcomes after a single-stage procedure for cell-based cartilage repair: a prospective clinical safety trial with 2-year follow-up. *Am J Sports Med*. 2011;39:1170–1179.
53. Christensen BB, Foldager CB, Jensen J, Lind M. Autologous dual-tissue transplantation for osteochondral repair: early clinical and radiological results. *Cartilage*. 2015;6:166–173.
54. Cugat R, Alentorn-Geli E, Navarro J, et al. A novel autologous-made matrix using hyaline cartilage chips and platelet-rich growth factors for the treatment of full-thickness cartilage or osteochondral defects: preliminary results. *J Orthop Surg (Hong Kong)*. 2020;28:2309499019887547.
55. Lorenz CJ, Freislederer F, Salzmann GM, Scheibel M. Minced cartilage procedure for one-stage arthroscopic repair of chondral defects at the glenohumeral joint. *Arthrosc Tech*. 2021;10:e1677–e1684.
56. Roth KE, Klos K, Simons P, et al. Cartilage chip transplantation for cartilage defects of the first metatarsophalangeal joint. *Oper Orthop Traumatol*. 2021;33:480–486.
57. Schumann J, Salzmann G, Leunig M, Rudiger H. Minced cartilage implantation for a cystic defect on the femoral head-technical note. *Arthrosc Tech*. 2021;10:e2331–e2336.
58. Adkisson HD, Gillis MP, Davis EC, Maloney W, Hruska KA. *In vitro* generation of scaffold independent neocartilage. *Clin Orthop Relat Res*. 2001. doi:10.1097/00003086-200110001-00026S280-294.
59. Adkisson HD, Martin JA, Amendola RL, et al. The potential of human allogeneic juvenile chondrocytes for restoration of articular cartilage. *Am J Sports Med*. 2010;38:1324–1333.
60. Farr J, Cole BJ, Sherman S, Karas V. Particulated articular cartilage: CAIS and DeNovo NT. *J Knee Surg*. 2012;25:23–29.
61. Farr J, Yao JQ. Chondral defect repair with particulated juvenile cartilage allograft. *Cartilage*. 2011;2:346–353.
62. Riboh JC, Cole BJ, Farr J. Particulated articular cartilage for symptomatic chondral defects of the knee. *Curr Rev Musculoskelet Med*. 2015;8:429–435.
63. Wang T, Belkin NS, Burge AJ, et al. Patellofemoral cartilage lesions treated with particulated juvenile allograft cartilage: a prospective study with minimum 2-year clinical and magnetic resonance imaging outcomes. *Arthroscopy*. 2018;34:1498–1505.
64. Waterman BR, Waterman SM, McCriskin B, Beck EC, Graves RM. Particulated juvenile articular cartilage allograft for treatment of chondral defects of the knee: short-term survivorship with functional outcomes. *J Surg Orthop Adv*. 2021;30:10–13.
65. Manzi J, Arzani A, Hamula MJ, Manchanda K, Dhanaraj D, Chapman CB. Long-term patient-reported outcome measures following particulated juvenile allograft cartilage implantation for treatment of difficult osteochondral lesions of the talus. *Foot Ankle Int*. 2021;42:1399–1409.
66. Niemeyer P, Laute V, Zinser W, et al. A prospective, randomized, open-label, multicenter, phase iii noninferiority trial to compare the clinical efficacy of matrix-associated autologous chondrocyte implantation with spheroid technology versus arthroscopic microfracture for cartilage defects of the knee. *Orthop J Sports Med*. 2019;7:2325967119854442.
67. Brittberg M, Recker D, Ilgenfritz J, Saris DBF, Group SES. Matrix-applied characterized autologous cultured chondrocytes versus microfracture: five-year follow-up of a prospective randomized trial. *Am J Sports Med*. 2018;46:1343–1351.
68. Saris D, Price A, Widuchowski W, et al. Matrix-applied characterized autologous cultured chondrocytes versus microfracture: two-year follow-up of a prospective randomized trial. *Am J Sports Med*. 2014;42:1384–1394.
69. Zeifang F, Oberle D, Nierhoff C, Richter W, Moradi B, Schmitt H. Autologous chondrocyte implantation using the original periosteum-cover technique *versus* matrix-associated autologous chondrocyte implantation: a randomized clinical trial. *Am J Sports Med*. 2010;38:924–933.
70. Akgun I, Unlu MC, Erdal OA, et al. Matrix-induced autologous mesenchymal stem cell implantation versus matrix-induced autologous chondrocyte implantation in the treatment of chondral defects of the knee: a 2-year randomized study. *Arch Orthop Trauma Surg*. 2015;135:251–263.
71. Wondrasch B, Risberg MA, Zak L, Marlovits S, Aldrian S. Effect of accelerated weightbearing after matrix-associated autologous chondrocyte implantation on the femoral condyle: a prospective, randomized controlled study presenting MRI-based and clinical outcomes after 5 years. *Am J Sports Med*. 2015;43:146–153.
72. Niemeyer P, Laute V, John T, et al. The effect of cell dose on the early magnetic resonance morphological outcomes of autologous cell implantation for articular cartilage defects in the knee: a randomized clinical trial. *Am J Sports Med*. 2016;44:2005–2014.
73. Minas T, Gomoll AH, Rosenberger R, Royce RO, Bryant T. Increased failure rate of autologous chondrocyte implantation after previous treatment with marrow stimulation techniques. *Am J Sports Med*. 2009;37:902–908.