WASHINGTON STATE HEALTH CARE AUTHORITY

Osteochondral Allograft/Autograft Transplantation (OAT)

Health Technology Assessment

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Health Technology Assessment Program

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Osteochondral Allograft/Autograft Transplantation (OAT)

Provided by:

Spectrum Research, Inc.

APPENDICES

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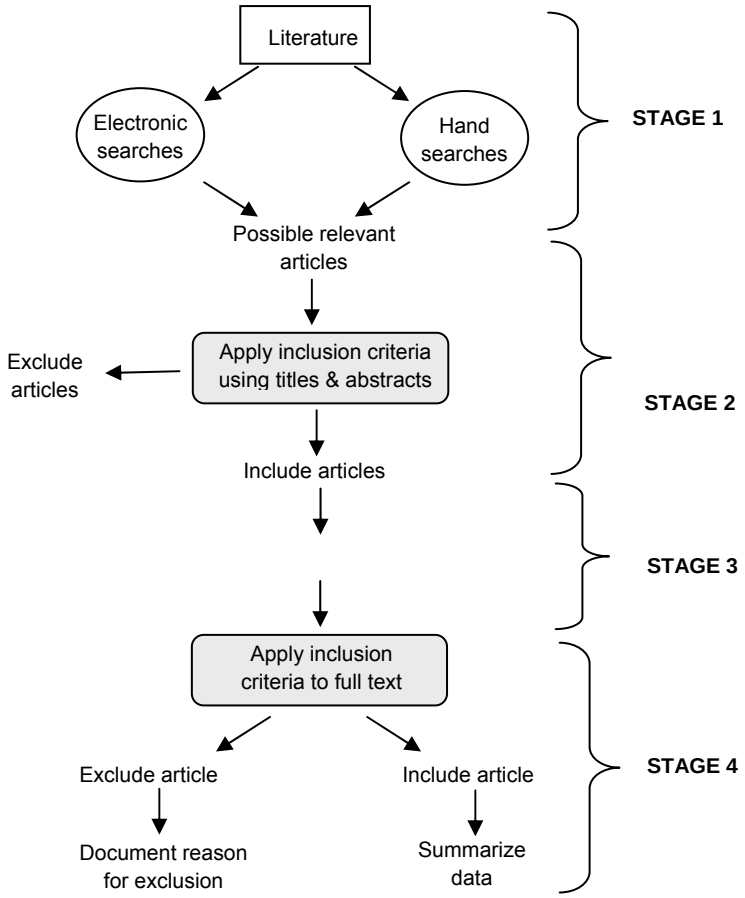
Appendix A. Algorithm for Article Selection



Appendix B. Search Strategy

Search performed through 06-21-11

PubMed Search strategy:

Limits Activated: only items with abstracts, Humans, English

	Search terms	Number of articles
#1	("osteochondral autograft transfer" OR "mosaicplasty" OR "mosaicplasties")	111
#2	(chondral OR osteochondral) OR ("Cartilage, Articular"[MeSH] OR "Osteochondritis Dissecans"[MeSH] OR "osteochondritis dissecans")	9959
#3	#1 OR #2	9962
#4	(transplant OR transplants OR transplantation* OR implant OR implants OR implantation* OR graft OR grafts OR grafting OR autograft* OR autologous OR autotransplant* OR ("Transplantation, Autologous"[MeSH]) OR allograft* OR allogeneic OR homograft* OR allotransplant* OR ("Transplantation, Homologous"[MeSH]))	395,665
#5	#3 AND #4	1647
#6	rabbit* OR "mouse" OR "mice" OR "rat" OR "rats" OR "dog" OR "dogs" OR "Models, Animal"[MeSH] OR (Animals[MeSH] NOT "Humans"[MeSH])	463,200
#7	("Case Reports"[Publication Type] OR "case report")	659,066
#8	#6 OR #7	1,116,561
#9	#1 OR #5 NOT #8	1255

These 1255 citations formed the basis of the citation list were searched and categorized based on study type and applicability to key questions within an EndNote Library. The titles and abstracts for all citations were evaluated by at least one investigator and a minimum of two investigators made final inclusion/exclusion decisions. Hand searches of included studies were performed and generally revealed no studies that met the inclusion criteria that were not captured by this broad search for key questions 3-6.

Additional searches for specific key questions

Key Question1

Broad search above yielded 16 potential citations

Additional terms/strategy

	Search terms	Number of articles
#1	(chondral OR osteochondral) OR ("Cartilage, Articular"[MeSH] OR "Osteochondritis Dissecans"[MeSH] OR "osteochondritis dissecans")	21376
#2	Radiography"[Mesh]	552979
#3	#1 OR #2	
#4	SENSITIVITY[TIAB] OR SPECIFICITY[TIAB] OR PREDICT*[TIAB] OR "Reproducibility of Results"[Mesh] OR RELIAB*[TI] OR VALID* OR INTERTEST* OR INTEROBSERV* OR INTRATEST* OR INTRAOBSERV* OR INTERRAT* OR INTRARAT* OR "Validation Studies" [Publication Type] OR "Reproducibility of Results"[Mesh]	1647906

	Limits: only items with abstracts, Humans, English	
#5	#3 AND #4	138
#6	(valid* OR reliable OR reliability)	
#7	"Diagnosis"[Mesh] AND Search (chondral OR osteochondral) OR ("Cartilage, Articular"[MeSH] OR "Osteochondritis Dissecans"[MeSH] OR "osteochondritis dissecans")	21350
#8	#6 AND # 7 Limits: only items with abstracts, Humans, English	494
#9	#6 AND #7 NOT (menisc* OR ligament* OR osteoarthritis OR arthritis OR hip OR acetabul* OR spine) Limits: only items with abstracts, Humans, English	210
#10	"Decision Making"[Mesh]AND (chondral OR osteochondral) OR ("Cartilage, Articular"[MeSH] OR "Osteochondritis Dissecans"[MeSH] OR "osteochondritis dissecans") Limits: Humans, English	10833
#11	#10 AND treatment	4615
#12	#10 and (transplant OR transplants OR transplantation* OR implant OR implants OR implantation* OR graft OR grafts OR grafting OR autograft* OR autologous OR autotransplant* OR ("Transplantation, Autologous"[MeSH]) OR allograft* OR allogeneic OR homograft* OR allotransplant* OR ("Transplantation, Homologous"[MeSH])) Limits: abstracts. Humans, English	1301
	Potentially relevant citations (unique from broad PubMed search)	**36**

Additional searches were done on the lesions classification systems with these results: From 12 potentially relevant citations, 2 were evaluated further.

- "Outerbridge classification" AND (valid* OR reliable OR reliability) = 5 hits – 1 of 5 included
- "Noyes classification" AND (valid* OR reliable OR reliability) = 1 hit – 0 of 1 included
- "ICRS classification" AND (valid* OR reliable OR reliability) = 1 hit – 1 of 1 included
- "ICRS OCD classification" AND (valid* OR reliable OR reliability) = 0 hits – 0 of 0 included
- "Fairbank classification" AND (valid* OR reliable OR reliability) = 3 hits – 0 of 3 included
- "Hepple classification" AND (valid* OR reliable OR reliability) = 3 hits – 0 of 3 included
- "Ferkel classification" AND (valid* OR reliable OR reliability) = 0 hits – 0 of 0 included

Hand search of bibliographies: 7 additional potentially relevant articles that were unique citations.

Key Question 2

To identify outcomes measures tested for validity, reliability or responsiveness in an osteochondral population, searches on the measures used in included comparative studies were performed. Of 93 citations, only 6 were potentially relevant (i.e described testing in the population of interest and were further evaluated. An additional 3 were considered based on the first broad search of 1255.

- ("Cincinnati knee" OR Cincinnati knee rating") AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 5 hits – 0 of 5 tested
- ("Modified Cincinnati knee" OR Modified Cincinnati knee rating") AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 4 hits – 1 of 4 tested

- (“knee injury and osteoarthritis score” OR KOOS) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 11 hits – 1 of 11 tested
- (“International Cartilage Repair Society” OR ICRS) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 17 hits – 2 of 17 tested
- (“Hospital for special surgery score” OR HSSS) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 6 hits – 0 of 6 tested
- (“Meyers score”) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 0 hits
- (Lysholm) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 10 hits – 1 of 10 tested
- (“Modified Lysholm”) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 4 hits – 0 of 4 tested
- (“International knee documentation committee” OR IKDC) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 14 hits 1 of 14 tested
- (“Tegner activity scale”) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 2 hits – 0 of 2 tested
- (“International Cartilage Repair Society” OR ICRS) AND functional) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 7 hits – 0 of 7 tested
- (“International Cartilage Repair Society” OR ICRS) AND activity level) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 1 hit – 0 of 1 tested
- (sf-36 OR “Short form 36”) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 10 hits – 0 of 10 tested
- (sf-12 OR “Short form 12”) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 0 hits
- (“Pain disability index” OR PDI) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) 0 hits
- (EQ-5D) AND (osteochondral OR chondral OR focal OR "cartilage repair") AND (valid* OR reliab* OR responsive*) = 2 hits – 0 of 2 hits

One study, Briggs (2006), was found after looking through the references of similar studies.

Appendix C. Articles Excluded at Full-Text Review

Procedure not similar to OATS or is not clear

Dick, H. M., T. I. Malinin, et al. (1985). "Massive allograft implantation following radical resection of high-grade tumors requiring adjuvant chemotherapy treatment." Clin Orthop Relat Res(197): 88-95

Colangeli, M., D. Donati, et al. (2007). "Total knee replacement versus osteochondral allograft in proximal tibia bone tumours." Int Orthop **31**(6): 823-829.

Sim, F. H., C. P. Beauchamp, et al. (1987). "Reconstruction of musculoskeletal defects about the knee for tumor." Clin Orthop Relat Res(221): 188-201.

Giannini, S., R. Buda, et al. "Bipolar fresh osteochondral allograft of the ankle." Foot Ankle Int **31**(1): 38-46

Davidson, P. A., D. W. Rivenburgh, et al. (2007). "Clinical, histologic, and radiographic outcomes of distal femoral resurfacing with hypothermically stored osteoarticular allografts." Am J Sports Med **35**(7): 1082-109

Gerrand, C. H., A. M. Griffin, et al. (2003). "Large segment allograft survival is improved with intramedullary cement." J Surg Oncol **84**(4): 198-208.

Kandel, R. A., A. E. Gross, et al. (1985). "Histopathology of failed osteoarticular shell allografts." Clin Orthop Relat Res(197): 103-110.

Muscolo, D. L., M. A. Ayerza, et al. (2008). "Unicondylar osteoarticular allografts of the knee. Surgical technique." J Bone Joint Surg Am **90 Suppl 2 Pt 2**: 206-217.

Oakeshott, R. D., I. Farine, et al. (1988). "A clinical and histologic analysis of failed fresh osteochondral allografts." Clin Orthop Relat Res(233): 283-294

Jeng, C. L., A. Kadakia, et al. (2008). "Fresh osteochondral total ankle allograft transplantation for the treatment of ankle arthritis." Foot Ankle Int **29**(6): 554-560.

Draper, S. D. and L. M. Fallat (2000). "Autogenous bone grafting for the treatment of talar dome lesions." J Foot Ankle Surg **39**(1): 15-23.

Stone, K. R., A. W. Walgenbach, et al. (2006). "Articular cartilage paste grafting to full-thickness articular cartilage knee joint lesions: a 2- to 12-year follow-up." Arthroscopy **22**(3): 291-299

Validation/reliability studies – not evaluating osteochondral defects or outcomes not separated or non-human studies or doesn't address question

Irrgang JJ, Anderson AF, Boland AL, et al (2001) Development and validation of the international knee documentation committee subjective knee form. Am J Sports Med; 29:600-613.

Irrgang JJ, Anderson AF, Boland AL, et al (2006) Responsiveness of the International Knee Documentation Committee Subjective Knee Form. Am J Sports Med; 34:1567-1573.

Marx RG, Jones EC, Allen AA, et al (2001) Reliability, validity, and responsiveness of four knee outcome scales for athletic patients. J Bone Joint Surg Am;1459-1469.

Cameron, M. L., K. K. Briggs, et al. (2003). "Reproducibility and reliability of the outerbridge classification for grading chondral lesions of the knee arthroscopically." Am J Sports Med **31**(1): 83-86.

Javed, A., M. Siddique, et al. (2002). "Interobserver variations in intra-articular evaluation during arthroscopy of the knee." J Bone Joint Surg Br **84**(1): 48-49.

Oakley, S. P., I. Portek, et al. (2003). "Accuracy and reliability of arthroscopic estimates of cartilage lesion size in a plastic knee simulation model." Arthroscopy **19**(3): 282-289.

Briggs, T. W., S. Mahroof, et al. (2003). "Histological evaluation of chondral defects after autologous chondrocyte implantation of the knee." J Bone Joint Surg Br **85**(7): 1077-1083.

Hambly, K., V. Bobic, et al. (2006). "Autologous chondrocyte implantation postoperative care and rehabilitation: science and practice." Am J Sports Med **34**(6): 1020-1038.

Kocher, M. S., J. DiCanzio, et al. (2001). "Diagnostic performance of clinical examination and selective magnetic resonance imaging in the evaluation of intraarticular knee disorders in children and adolescents." Am J Sports Med **29**(3): 292-296.

Luhmann, S. J., M. Schootman, et al. (2005). "Magnetic resonance imaging of the knee in children and adolescents. Its role in clinical decision-making." J Bone Joint Surg Am **87**(3): 497-502.

Outcomes not separated for OATS/mosaicplasty

Noyes, F. R., S. D. Barber-Westin, et al. (2004). "Meniscal transplantation in symptomatic patients less than fifty years old." J Bone Joint Surg Am 86-A(7): 1392-1404

Autograft Series >30: not report on complications

Radulescu, R. A., C. F. Cirstoiu, et al. "Arthroscopical and histological study of cartilaginous lesions treated by mosaicplasty." J Med Life 3(4): 407-411.

Marcacci, M., E. Kon, et al. (2007). "Arthroscopic second generation autologous chondrocyte implantation." Knee Surg Sports Traumatol Arthrosc 15(5): 610-619.

Kokkinakis, M., K. Kafchitsas, et al. (2008). "Is MRI useful in the early follow-up after autologous osteochondral transplantation?" Acta Orthop Belg 74(5): 636-642

Appendix D. Methods for LoE and SoE Determination

Methods for critical appraisal and level of evidence assessment

The method used for assessing the quality of evidence of individual studies as well as the overall quality of evidence incorporates aspects of rating scheme developed by the Oxford Centre for Evidence-based Medicine, [Phillips] precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group [Atkins, 2004] and recommendations made by the Agency for Healthcare Research and Quality (AHRQ) [West]. Taking into account features of methodological quality and important sources of bias combines epidemiologic principles with characteristics of study design.

Procedures for determining adherence to level of evidence (LoE) criteria

Each study was rated against pre-set criteria that resulted in an evidence rating (Level of Evidence I, II (IIa or IIb), III, or IV) and presented in a table. For therapeutic and prognostic articles, the criteria are listed in the Table below. All criteria met are marked. A "+" signifies that the criterion was present, a "–" indicates that the criterion was not present, and "+/–" indicates that the reviewers could not be determine whether the criterion was met.

After the Level of Evidence was judged, the study could be upgraded or downgraded using the following:

Upgrade: Large effect size, dose response
Downgrade: limitations in study execution, indirectness of evidence

Definition of the different levels of evidence for articles on therapy and prognosis

	Studies of Therapy		Studies of Prognosis	
Level	**Study design**	**Criteria**	**Study design**	**Criteria**
I	Good quality RCT	• Random sequence generation • Allocation concealment • Intent-to-treat analysis • Blind or independent assessment for important outcomes • Co-interventions applied equally • F/U rate of 80%+ • Adequate sample size	Good quality cohort	• Prospective design • Patients at similar point in the course of their disease or treatment • F/U rate of 80%+ • Patients followed long enough for outcomes to occur • Controlling for extraneous prognostic factors*
II	Moderate (IIa) or Poor (IIb) quality RCT	• Violation of one of the criteria for good quality RCT • Violation of two or more criteria for a good quality RCT	Moderate quality cohort	• Prospective design, with violation of one of the other criteria for good quality cohort study
	Good quality cohort	• Blind or independent assessment in a prospective study, or use of reliable data* in a retrospective study • Co-interventions applied equally • F/U rate of 80%+ • Adequate sample size • Controlling for possible confounding†		• Retrospective design, meeting all the rest of the criteria in level I
III	Moderate or poor quality cohort	• Violation of any of the criteria for good quality cohort	Poor quality cohort	• Prospective design with violation of 2 or more criteria for good quality cohort, or • Retrospective design with violation of 1 or more criteria for good quality cohort
	Case-control	• Any case-control design	Case-control	• Any case-control design
IV	Case series	• Any case series design	Case series	• Any case series design

*Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Assessment of HTAs, systematic reviews and meta-analyses

If such reports are used as the primary data/evidence for a given topic, the following checklist is used to assess the quality of each included report

Assessment check list for HTAs, systematic reviews and meta-analyses

Methodological Principle*	
Purpose, aim, study question, and/or hypothesis stated	
Literature search described	
Unpublished sources sought	
Inclusion/exclusion criteria stated	
Characteristics of included studies provided	
Quality of included studies formally assessed and method described	
Overall quality of included studies (LoE) given primary purpose/aim	
Quantitative analysis	
• Studies appraised critically	
• Magnitude and direction of effect sizes evaluated	
• Consistency of effect sizes evaluated	
• Stability of effect sizes (e.g. confidence intervals) evaluated	
• Scientific quality of studies considered in conclusions	
• Methods to enhance objectivity incorporated	
Quantitative analysis	
• Heterogeneity evaluated	
• Heterogeneity explored, if present	
• Missing data handled appropriately	
• Effect sizes pooled appropriately	
• Sensitivity analysis conducted	
• Publication bias explored	
Potential conflict of interest stated	

Description of Methodological Principle for SRs and HTAs

Report type:
The type and purpose of the report influence the extent to which some of the factors listed above are applicable. For instance, for some purposes, quantitative analysis and statistical pooling may not be possible, necessary or appropriate.

Health Technology Assessments (HTAs) and similar reports are those which systematically evaluate the effectiveness, safety, cost implications and other properties of technology use (frequently therapeutic or diagnostic technologies) in health care, generally with respect to competing alternatives. HTA methods generally include formal systematic search for and critical appraisal of medical literatures and may include meta-analytic techniques for combining data across studies. HTAs and similar reports are frequently done by governmental agencies and/or commissioned by such agencies from private vendors. The primary purpose is to advise or inform technology-related decision and policy-making in a variety of settings, including individual (e.g. patient and/or provider) and institutional (provider organizations, health plans, government agencies) on local, regional, national or international levels.

Systematic review is a general term used to describe focused summaries of medical literature to address specific clinical questions using explicit strategies for literature search, inclusions and exclusions of studies and documentation of processes used to find and summarize data from the medical literature. Systematic reviews may or may not include formal meta-analysis and pooling of data.

Meta-analysis is a term used for systematic reviews which use quantitative, statistical methods to pool data to summarize results across studies. A systematic review generally forms the basis of meta-analysis in that a formally systematic approach to finding and selecting relevant studies for summarization is done. Pooling of data across studies may enhance statistical power to detect differences between groups. The quality of the studies to be pooled and potential for bias based on methodological flaws in individual studies needs to be considered. Methods for pooling studies (or individual patient data from a number of studies) should be stated and appropriate for the types of data and studies from which they come. Heterogeneity across studies can compromise the credibility of the pooled estimate. Heterogeneity can be related to clinical, patient or study characteristics which may or may not manifest in statistical heterogeneity. Formal evaluation and exploration of statistical heterogeneity should be done using accepted methods and modeling done accordingly (e.g. use of random effects model instead of fixed model). In evidence-based medicine, meta-analyses of the highest quality studies (usually RCTs) is considered to the highest level of evidence, however, limitations of meta-analysis should also be considered.

Pooled analyses frequently combine outcomes from individual patients enrolled in primary studies, the patient is the unit of analysis. These analyses may not be part of a complete systematic review of the literature. As with meta-analyses, tests for homogeneity should be done and the basis of pooling should be well described.

Criteria:

1. **Purpose, aim,** study (or key) questions and/or hypothesis for the report or analysis should be stated clearly.

2. **The literature search** should be described including timing of the search, data sources searched and search strategies used.

3. **Inclusion and exclusion criteria** for include studies should be stated and relevant to the purpose and questions to be addressed in the report and consistent with accepted methods for conduct of the type of report.

4. **Characteristics of included studies** should be given with regard to study design, populations studied and technologies applied as relevant to the report's purpose and aims.

5. **Quality of included studies** should be formally assessed using a specified system for evaluation that takes into account study design, potential sources of bias, methodological limitations, statistically power and use of appropriate analyses (e.g. controlling for confounding), usually leading to an overall score, classification or grade of evidence.

6. **The Level of Evidence (LoE)** of individual studies included should be the highest possible based on the primary focus of the report. Spectrum Research's LoE criteria are described below. If all included studies are RCTs (randomized controlled trials), the LoE using Spectrum Research's approach is either I or II. For trials of surgery or other interventions where clinician and/or patients are not blinded, the LoE is often II, since there is the opportunity for bias in assessment by the clinician and/or bias in patient response. Whether this criterion is met depends on the primary outcome and whether it could have been assessed in a blinded fashion. Subanalyses of RCTS are considered LoE II/III since randomization is generally not preserved. Registry studies are primarily retrospective cohort studies and subject to bias from a variety of sources and are classified as LoE III.

7. **Qualitative analysis:** Some reports may primarily provide qualitative assessment of included studies. Systematic reviews and meta-analyses should incorporate most of these components. The extent to which the following criteria are met provides some indication of the overall quality of the assessment

    - **Critical appraisal of included studies** – The report should describe a formal method of evaluating individual quality with regard to study design, methodological issues and potential for bias, such as the LoE system described below. A "grade" or other classification of study quality should be described and applied across studies.
    - **Evaluation of estimate magnitude and direction:** The report should accurately interpret and describe these, including statistical significance and any statistical adjustments to effect size estimates.
    - **Estimate consistency**: Reports should describe the general patterns of effect size estimates across studies and how consistent they are. Reports should describe if estimates from different studies have the same general direction and magnitude across studies or not.
    - **Estimate stability**: Reports should comment on the general stability of estimates, based in consideration of things like confidence intervals, effects of missing data, study sample size, confounding and other factors which may influence estimate stability
    - Consideration of the **overall scientific quality** of the evidence for a specific question: Do the report's conclusions consider the overall strength of evidence based on the scientific quality of the studies, the consistency, direction and magnitude of the estimates used to formulate the conclusions?

8. **Quantitative analysis: T**his involves the statistical combining and evaluation of data from multiple studies and applies to situations where meta analysis is done.
    - **Pooling** of data may or may not be appropriate depending on the types of studies and data available. Various methods for pooling data are possible. The report should adequately describe how pooling was done and methods used to create summary estimates should be appropriate to the data, included studies and consideration of factors such as clinical and statistical heterogeneity. Methods for study weighting and modeling of pooled estimates should be described.

  - Formal meta-analysis is a structured process with specific types of methodologies for combining data, weighting studies, modeling and assessing heterogeneity across studies in order to arrive at pooled estimates of effect size.
  - Not all reports that pool data across studies are true meta-analyses from a methodological perspective.
- **Evaluation of heterogeneity**. Description of how heterogeneity was evaluated should be consistent with the type of analysis and modeling done to pool the data and specific criteria for determining heterogeneity should be described and applied. The results of heterogeneity evaluations should be stated.
- **Exploration of heterogeneity if present**: If there is significant heterogeneity present, a description of possible sources and methods used to explore it should be described and the results reported.
- **Missing data:** Does the report describe missing data, how it was handled and the extent to which it may influence estimate stability, which may in part be done with sensitivity analysis
- **Sensitivity analysis:** The report should explore the stability of estimates using appropriate sensitivity analyses, including around missing data or areas of heterogeneity. Exploration of publication bias should be described as appropriate.

9. **Potential conflicts of interest:** Is the source of funding for the report stated and/or is there information on potential conflicts of interest for authors presented?

Determination of Overall Strength of Evidence

Following the assessment of the quality of each individual study included in the report, an overall "strength of evidence for the relevant question or topic is determined. Methods for determining the overall strength of evidence for diagnostic studies are variable across the literature and are most applicable to evaluation of therapeutic studies.

SRI's method incorporates the primary domains of quality (LoE), quantity of studies and consistency of results across studies as described by AHRQ[215].

SRI establishes a strength-of-evidence baseline using the following definitions to determine whether or not the body or evidence meets the criteria for each domain:

Domain	Definition/Criterion
Quality	• At least 80% of the studies are LoE I or II
Quantity	• There are at least three studies which are adequately powered to answer the study question
Consistency	• Study results would lead to a similar conclusion (similar values, in the same direction) in at least 70% of the studies

Based on the criteria described above, the possible scenarios that would be encountered are described below. Each scenario is ranked according to the impact that future research is likely to

have on both the overall estimates of an effect and the confidence in the estimate. This ranking describes the overall "Strength of Evidence" (SoE) for the body of literature on a specific topic. The method and descriptions of overall strength are adapted for diagnostic studies from system described by the GRADE Working Group[12] for the development of clinical guidelines.

SoE	Description	Further Research Impact	Domain Criterion Met		
			Quality	Quantity	Consistency
1	**High**	Very unlikely to change confidence in effect estimate	+	+	+
2	**Moderate**	Likely to have an important impact on confidence in estimate and *may* change the estimate	+	-	+
			+	+	-
3	**Low**	Very likely to have an important impact on confidence in estimate and *likely* to change the estimate	+	-	-
			-	+	+
4	**Very Low**	Any effect estimate is uncertain	-	+	-
			-	-	+
			-	-	-

Limitations or special strengths can modify the quality of the evidence from the baseline as follows:

Factors that can reduce the quality of the evidence 1 or 2 levels:

- Limitations in study design or execution
- Indirectness of evidence
- Imprecision

Factors that can increase the quality of the evidence: 1 or 2 levels:

- Large magnitude of effect
- Dose response gradient

Assessment of Economic Studies

Full formal economic analyses evaluate both costs and clinical outcomes of two or more alternative interventions. The four primary types are cost minimization analysis (CMA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA), and cost-benefit analyses (CBA). Each employs different methodologies, potentially complicating critical appraisal, but some common criteria can be assessed across studies.

No standard, universally accepted method of critical appraisal of economic analyses is currently in use. A number of checklists [Canadian, BMJ, AMA] are available to facilitate critique of such

studies. The Quality of Health Economic Studies (QHES) instrument developed by Ofman, et al [Ofman] QHES embodies the primary components relevant for critical appraisal of economic studies [Chiou]. It also incorporates a weighted scoring process and which was used as one factor to assess included economic studies. This tool has not yet undergone extensive evaluation for broader use but provides a valuable starting point for critique.

In addition to assessment of criteria in the QHES, other factors are important in critical appraisal of studies from an epidemiologic perspective to assist in evaluation of generalizability and potential sources of study bias.

Such factors include:

- Are the interventions applied to similar populations (eg, with respect to age, gender, medical conditions, etc)? To what extent are the populations for each intervention comparable and are differences considered or accounted for? To what extent are population characteristics consistent with "real world" applications of the comparators?
- Are the sample sizes adequate so as to provide a reasonable representation of individuals to whom the technology would be applied?
- What types of studies form the basis for the data used in the analyses? Data (eg, complication rates) from randomized controlled trials or well-conducted, methodologically rigorous cohort studies for data collection are generally of highest quality compared with case series or studies with historical cohorts.
- Were the interventions applied in a comparable manner (eg, similar protocols, follow-up procedures, evaluation of outcomes, etc)?
- How were the data and/or patients selected or sampled (eg, a random selection of claims for the intervention from a given year/source or all claims)? What specific inclusion/exclusion criteria or processes were used?
- Were the outcomes and consequences of the interventions being compared comparable for each? (e.g., were all of the relevant consequences/complications for each intervention considered or do they primarily reflect those for one intervention?)

Assessment of the overall strength of evidence for formal economic analyses does not appear to be documented in the literature. For the purposes of this HTA, overall strength was determined by:

- Quality of the individual studies: Where the majority of quality indicators described in the QHES met and were the methods related to patient/claim selection, patient population considerations and other factors listed above consistent with a high quality design?
- Number of formal analyses (3 or more)
- Consistency of findings and conclusions from analyses across studies.

QHES Instrument **Study** _____

Questions	Points	Yes	No
1. Was the study objective presented in a clear, specific, and measurable manner?	7		
2. Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		
3. Were variable estimates used in the analysis from the best available source (ie, randomized controlled trial - best, expert opinion - worst)?	8		
4. If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1		
5. Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		
6. Was incremental analysis performed between alternatives for resources and costs?	6		
7. Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		
8. Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7		
9. Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		
10. Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included?	6		
11. Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7		
12. Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8		
13. Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7		
14. Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		
15. Were the conclusions/recommendations of the study justified and based on the study results?	8		
16. Was there a statement disclosing the source of funding for the study?	3		
TOTAL POINTS	**100**		

Appendix E. Level of Evidence (LoE) Ratings – Comparative Studies

Randomized Controlled Trials

Table E1: Methodological quality of therapeutic studies evaluating efficacy following OATS/mosiacplasty

Methodological principle	Bentley	Dozin	Gudas 2005	Gudas 2009	Horas
Randomized controlled trial	+	+	+	+	quasi
→ Random sequence generation	+	+	-	+	-
→ Allocation concealment	-	+	-	-	-
→ Intention to treat	+	+	+	+	+
Cohort study					
Case series					
Independent or blind assessment	-	-	+	-	-
Co-interventions applied equally	+	+	+	-	+
Complete follow-up of ≥ 80%	+	-	+	+	-
Adequate sample size	-	-	+	+	+
Controlling for possible confounding†	-	+/-	+	+	-
Evidence class	**IIb**	**IIb**	**IIb**	**IIb**	**IIb**

†Groups must be comparable on baseline characteristics or evidence of control for confounding presented.

Bentley

- Random sequence generation: credit, "patients were randomized to have either mosaicplasty or ACI…If the lesion was suitable for cartilage grafting, randomization was undertaking by using random sample numbers in sealed envelopes."
- Allocation concealment: no credit given, "randomization was undertaking by using random sample numbers in sealed envelopes." (no mention of the envelopes being opaque)
- Intent to treat: yes, though not mentioned, data appears to have been handled in a manner consistent with the intent to treat principle
- Independent or blind assessment: no, the primary outcome (Cincinnati rating system) is clinician-based; there is no mention that the assessor was blinded and there may have been differences in the appearance of the knees since different closure techniques were used.
- Co-interventions applied equally: credit, "the rehab program was identical after both operative techniques" (and subsequent text supports this). Note that while mosaicplasty was performed as a one-stage procedure and ACI as a two-stage procedure, the first stage of the ACI involved cartilage removal for cell culture only (but not debridement of the lesion).
- Complete f/u of ≥ 80%: credit (100%, see Table III)
- Adequate sample size: no, primary results (% of pts with excellent or good outcomes. Table III) were similar in both tx groups ($P = .277$); no mention of how adequate sample size was ensured/determined.
- Controlling for possible confounding: no, dissimilar distribution of etiology of defects and anatomical distribution; defect sizes not reported for each group (which could make a big difference in outcome); all but 6 pts had undergone prior surgeries but the # of these pts for each group was not reported. (no multivariate or stratified analysis was done).

Dozin

- Random sequence generation: yes, "…eligible patients were prospectively registered by phone through the Coordinating Center. Random treatment assignment was performed on the basis of random lists stratified by orthopedic surgeon and balanced in permuted blocks of varying block size in random sequence."

- Allocation concealment: yes, "random lists were kept at the Coordinating Center, and the clinical investigators were unaware of the sequence of the assignments. After verification of eligibility, the treatment assignment was communicated by phone to the orthopedic surgeon."
- Intent to treat: yes, patients who "spontaneously" recovered and did not receive ACI or Mosaic appear to have been evaluated in their assigned tx group (Table 3, 4).
- Independent or blind assessment: no, primary outcomes were patient-reported (IDKC and LKSS) but "pts not blinded to their treatment assignment."
- Co-interventions applied equally: yes, rehab program similar b/w groups
- Complete f/u of ≥ 80%: no, the functional status during f/u could only be assessed in 33/47 pts (70%). In addition, in patients with missing observation at 12 months,the approach referred to as last observation carried forward was used, so the actual f/u is even lower than 70%.; additionally unclear how many were eligible, how many randomized of the eligible. Authors only state that " forty seven patients were registered" and the coordinating center.
- Adequate sample size: no, even though statistics were done to determine adequate sample size (40 patients needed but the number was increased to 60 to account for the expected spontaneous recovery in the 6 month interval between initial scope and debridement and ACI or OATS), only 47 pts were randomized and of these, 52% of randomized pts ended up receiving ACI or OATS.
- Controlling for possible confounding: partial credit: Table 1 shows dissimilar distribution of patients by sex between tx groups (ACI, 77% male; mosaic, 46% male); BUT all other characteristics were very similarly distributed b/w groups. No multivariate or stratified analysis.

Gudas 2005

- Random sequence generation: no, "eligible patients were randomized to 1 of 2 groups. The type of surgery a pt received was based on sealed envelopes… If a patient had a preference for the type of treatment, he or she was dropped from the study." (no other details)
- Allocation concealment: no, sealed envelopes used, no mention of opacity or any other details (such as sequential numbering)
- Intent to treat: yes, though not mentioned, data appears to have been handled in a manner consistent with the intent to treat principle
- Independent or blind assessment: yes, a blinded unbiased observer performed preoperative and follow-up examinations; primary outcomes were clinician reported (ICRS and HSS).
- Co-interventions applied equally: yes, all pts rec'd identical rehabilitation.
- Complete f/u of ≥ 80%: 57/60 pts had complete f/u
- Adequate sample size: yes, there is a big difference in the primary outcome b/w tx groups.
- Controlling for possible confounding: yes, similar distribution of baseline characteristics (including lesion size, sex, injury to surgery, etc). Described mostly in text format in the last paragraph before Operative Technique.

Gudas 2009

- Random sequence generation: yes, "the type of surgery a pt received was based on personal data. Random number generation was created with the SPSS statistical program. Final eligibility was determined after an arthroscopic examination of the osteochondral lesion. At the same arthroscopy, a randomly elected treatment method was applied."
- Allocation concealment: no, no mention of concealment at all.
- Intent to treat: yes, though not mentioned, data appears to have been handled in a manner consistent with the intent to treat principle
- Independent or blind assessment: no, "a knee function test was performed by the surgeon (not an independent reviewer);" the clinical outcome was clinician-reported (ICRS) but there was no info as to whether this person was blinded); the MRI findings were reported by a blinded and independent observer but MRI findings are less meaningful secondary outcomes.
- Co-interventions applied equally: yes, "patients were treated following an identical rehab program".
- Complete f/u of ≥ 80%: yes, 47/50 pts had complete f/u
- Adequate sample size: yes, there was a statistically meaningful difference in the primary outcome b/w tx groups at one year; sample size analysis was also done.

- Controlling for possible confounding: yes, similar distribution of baseline characteristics (including lesion size, sex, injury to surgery, etc). Described mostly in text format in the last paragraph before Operative Technique.

Horas (quasi-RCT)

- Random sequence generation: no, "the patients were randomly assigned to either group, with an alternating consecutive selection, after they had provided informed consent."
- Allocation concealment: no, no info
- Intent to treat: yes, though not mentioned, data appears to have been handled in a manner consistent with the intent to treat principle
- Independent or blind assessment: No, primary outcome measure was modification of Lysholm scoring scale, which is pt-reported.
- Co-interventions applied equally: yes, both groups rec'd same rehab. Note that while mosaicplasty was performed as a one-stage procedure and ACI as a two-stage procedure, the first stage of the ACI involved cartilage removal for cell culture only (but not debridement of the lesion).
- Complete f/u of ≥ 80%: No; unclear how many eligible and of those how many were randomized and if any were lost prior to or after randomization.. Authors only state that "a total of 40 patients wer included".
- Adequate sample size: yes, significant differences in Lysholm scores b/w tx groups
- Controlling for possible confounding: no, many differences in baseline characteristics b/w groups (see demographic abstraction table) that weren't controlled for with multivariate or stratified analysis. (Note that baseline characteristics are presented in the study's appendix).

LoE for non-randomized comparative studies

In all of the following cohort studies study treatment was based on lesion type and/or severity, leading to confounding by indication. Sample sizes were small in most studies.

Table E2: Methodological quality of therapeutic studies evaluating effectiveness

Methodological principle	Gaweda, Mazurkiewicz 2006	Gaweda, Patyra 2006	Salzmann 2009	Widuchoswki 2008	Pascual-Garrido 2011	Rue 2008
Randomized controlled trial						
Cohort study						
Prospective	■	■			■	■
Retrospective			■	■		
Case series						
Independent or blind assessment	-	-	-	-	-	-
Co-interventions applied equally	+	+	+	-	+	+
Complete follow-up of ≥ 80%	-	-	-	-	+	+
Adequate sample size	+	+	+	-	+	+
Controlling for possible confounding†	-	-	+	-	+	-
Evidence class	**III**	**III**	**III**	**III**	**III**	**III**

Table E3: Methodological quality cohort study evaluating effectiveness following OATS/mosaicplasty of the ankle

Methodological principle	Gobbi 2006
Randomized controlled trial	
→ Random sequence generation	-
→ Allocation concealment	-
→ Intention to treat	-
Cohort study	+
Case series	

Independent or blind assessment	+/-
Co-interventions applied equally	+
Complete follow-up of ≥ 80%	+
Adequate sample size	+
Controlling for possible confounding†	-
Evidence class	**III**

Table E4: Methodological quality of case series looking at prognostic factors

Methodological principle	Hangody 2010	Haasper 2008	Marcacci 2005	Baltzer 2005	Andres 2003
Study design					
Randomized controlled trial					
→ Random sequence generation*					
→ Allocation concealment*					
→ Intention to treat*					
Cohort study					
Case series	+	+	+	+	+
Other Methods Implementation					
Independent or blind assessment	-	-	-	-	-
Co-interventions applied equally	-	-	-	-	+
Complete follow-up of ≥ 80%	-	-	-	-	+
Adequate sample size	-	-	-	-	-
Controlling for possible confounding†	-	-	-	-	-
Evidence class	**IV**	**IV**	**IV**	**IV**	**IV**

*Applies to randomized controlled trials only;
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Definitions of the different levels of evidence for reliability studies

Level	Study type	Criteria
I	Good quality study	• Broad spectrum of persons with the expected condition • Adequate description of methods for replication • Blinded performance of tests, measurements or interpretation • Second test/interpretation performed independently of the first
II	Moderate quality	• Violation of any one of the criteria for a good quality study
III	Poor quality study	• Violation of any two of the criteria
IV	Very poor quality study	• Violation of all three of the criteria

Table E5: Assessment of level of evidence (LoE) for reliability studies (KQ1)

Methodological Principle	Niemeyer	Spahn	Marx
Broad spectrum of patients with expected condition			
Adequate description of methods for replication	■	■	

Blinded/independent comparison of tests/interpretations		■	■
Evidence Level	**III**	**II**	**III**

Table E6: Quality assessment of outcome measures evaluated in persons with osteochondral defects (KQ2)

	Validity			Reliability				
Instrument	**Content validity**	**Criterion validity**	**Construct validity**	**Internal consistency**	**Reproducibility**	**Floor/ceiling**	**Responsiveness**	**MCID**
Patient-reported outcomes								
International Knee Documentation Committee subjective knee form (IKDC SKF) [Greco]	NR	NR	NR	NR	-	+/-	+	+
Lysholm Knee Scoring Scale* (LKSS)[Kocher, Smith HJ 2009]	NR	NR	-	-	+/-	+/-	-	NR
Knee Injury Osteoarthritis Outcome Score (KOOS) [Bekkers]	NR	NR	-	-	-	-	-	NR
Modified Cincinnati Knee Rating Systen (MCKRS) [Greco]	NR	NR	NR	NR	-		+/-	+
Clinician-reported outcomes								
International Cartilage Repair Society (ICRS) cartilage repair assessment † [Smith GD 2005, Vandenborne 2007]	NR	NR	-	-	-	NR	NR	NR

Table adapted from Lodhia et al. (2011)[78] and Terwee et al. (2007)[122]
NR = not reported
"+" indicates criteria were met, "+/-" indicates the quality assessment was inadequate or indeterminate, "-" indicates the criteria were not met; NR indicates the quality assessment was not reported or performed.
*Two studies [Kocher, Smith HJ] evaluated the LKSS
†Two studies [Smith GD 2005, Vandenborne 2007] evaluated the ICRS cartilage repair assessment

Appendix F. Key Question 2: Additional Materials

Functional outcome measures used in OATS studies for the knee

Clinician-based outcome measures:

- The **Cincinnati Rating Scale (CRS)[1]** is based on six subscales: subjective, activity, examination, stability, radiographs, and function. The CRS has not been evaluated in an osteochondral population. It has been validated in a ligament injury population [2, 3].
- The **Knee Injury Osteoarthritis Outcome Score (KOOS)**[4] is based on five subscales: pain, symptoms, activities of daily living, sports/recreation, and quality of life. The KOOS has been found to be valid, reliable and responsive in an osteochondral population and is discussed in more detail in the tables belos [5].
- The **International Cartilage Repair Society (ICRS) cartilage repair assessment** [6, 7] is a measure based on three subscales: degree of defect repair, integration to border zone, and macroscopic appearance. The ICRS cartilage repair system has been shown to be valid and reliable in an osteochondral population and is discussed in more detail in table below [8, 9].
- The **Marshall Knee Score (MKS)** [10] is based on three subscales: subjective complaints, knee examination, and stability. The MKS has not been validated in an osteochondral population.
- The **Modified/Hospital for Special Surgery Score (HSSS)†**[11, 12] based on six subscales: pain, function, range of motion, strength, deformity and instability. Subtractions from score for use of assistive device, extension lag, or valgus/varus deformity. The HSSS has not been validated in an osteochondral population. It has been validated in an anterior cruciate ligament surgery and total knee arthroplasty population [3, 13].
- The **Meyers Score (MS)** [14] based on three subscales: pain, function, and range of motion. The MS has not been validated in an osteochondral population.

Patient-reported outcome measures:

- The **Modified Cincinnati Rating Scale (MCRS)*** a modification of the CRS with eight subscales: pain, giving way, swelling, walking, stair-walking, running, jumping, and overall activity. It has been found to be reliable and responsive in an osteochondral population and is discussed in more detail in table[15].
- The **Lysholm Knee Scoring Scale (LKSS)**[16] is most frequently used to evaluate function based on pain, instability, swelling, stair climbing and four additional subscales. The LKSS has been shown to be valid, reliable and responsive in an osteochondral population and is discussed in more detail in table [17-19]
- The **Modified Lysholm Score (MLS)**[20] is a modification of the score by Lysholm. Like the LKSS the modified LKSS is used to evaluate function based on pain, instability,

swelling, stair climbing and four additional subscales. One of these additional subscales, catching/locking replaced the atrophy subscale of the LKSS.

- The **Stanmore Functional Rating System (SFRS)[21]** is used to evaluate function by different levels of pain and activity. The SFRS has not been shown to be tested in an osteochondral population.
- The **International Knee Documentation Committee (IKDC) subjective knee form**[22] is based on symptoms, sports activities, and function. The IKDC subjective knee form has been shown to be reliable and responsive in an osteochondral population and is discussed in more detail in the table [15].
- The **Tegner Activity Scale (TAS)**[20] is intended to be used as a patient self-completed instrument. It separates recreational and competitive sporting activities because of risk and injury incidence are higher in competitive sports. The TAS has been found to have content validity in a meniscal lesion with intra-articular lesion population. However, it has not been tested for construct validity in an osteochondral population. Construct validity has been tested in ligament injury[20] and patellar dislocation[23] populations.
- The **International Cartilage Repair Society (ICRS) functional status**[24] is used to evaluate function by four different levels of ability to use affected joint. ICRS functional status has not been validated in an osteochondral population.
- The **International Cartilage Repair Society (ICRS) activity level**[24] is used to evaluate activity by four different levels: competitive sportsman, frequently sporting, sporting sometimes, and non-sporting. ICRS activity level has not been validated in an osteochondral population.
- The **Short Form-36 (SF-36)** [25] provides summary measures for physical and mental well-being, with standardized scores ranging from 0 to 100. The SF-36 has not been validated in an osteochondral population.
- The **Short Form-12 (SF-12)** [26] is an abbreviated version of the SF-36 and provides summary measures for physical and mental well-being, with standardized scores ranging from 0 to 100. The SF-12 has not been validated in an osteochondral population.
- The **Pain Disability Index (PDI)** [27] is based on seven equally weighted subscales. The PDI has not been validated in an osteochondral population.
- The **EuroQoL-5 Dimensions (EQ-5D)** [28] is based on five subscales: mobility, self-care, usual activity, pain, and anxiety/depression. The PDI has not been validated in an osteochondral population.

Table F1: Validity, reliability, and responsiveness of functional outcome measures

Outcome measure	Patient population tested in	Validity	Reliability	Responsiveness
Lysholm Knee Scoring Scale[16]	Patients with chondral disorders of the knee (N = 1657) (44 years; 61% male)[18]	+	+	Not tested
	Patients with arthroscopically documented chondral disorders of the knee (N = 57) (44 years; 61% male)[18]	Not tested	+	Not tested

	Patients with chondral injuries of the knee (N = 248) (40 years; 67% male)[18]	+	Not tested	+
	Patients with a meniscal lesion and associated intra-articular lesions (N = 477) (39 years; 77% male)[17]	+	+	Not tested
	Patients awaiting surgery with isolated symptomatic cartilage defects on the femoral condyle or trochlea (N = 157) (37 years; 67% male)[19]	+	+	Not tested
Knee Injury Osteoarthritis Outcome Score (KOOS)[4]	Patients with focal cartilage lesions treated with either autologous chondrocyte implantation (n = 20) or microfracturing (n = 20) (N = 40) (35 years; 70% male)[5]	+	+	+
International Knee Documentation Committee (IKDC) subjective knee form[22]	Patients who had undergone articular cartilage surgery 5 years prior (N = 17) (44 years; 62% male)[15]	Not tested	+	Not tested
	Patients diagnosed with focal articular cartilage defects (N = 51) (37 years; 61% male)[15]	Not tested	Not tested	+
Modified Cincinnati Rating Scale*	Patients who had undergone articular cartilage surgery 5 years prior (N = 17) (44 years; 62% male)[15]	Not tested	+	Not tested
	Patients diagnosed with focal articular cartilage defects (N = 51) (37 years; 61% male)[15]	Not tested	Not tested	+
International Cartilage Repair Society (ICRS) cartilage repair assessment[6, 7]	Images from patients that had undergone microfracture or autologous chondrocyte implantation (N = 101) (age: NR; sex: NR)[9]	+	+	Not tested
	Arthroscopic videos of patients assessed by panel of orthopedic surgeons specializing in cartilage repair (N = NR) (age: NR; sex: NR)[8]	+	+	Not tested

Table F2: Descriptions of outcomes instruments used in osteochondral studies.

Outcome measure	Clinician based or patient reported	Instrument type	Components	Score range	Interpretation
Knee					
Cincinnati Rating Scale (CRS)[1]	CBO	Disease specific	6 subscales (28 items with 8 completed by patient): • Subjective (20 points) • Activity level (15 points) • Examination (25 points) • Stability (20 points)	NR	Excellent: All subscales grade excellent (may have one in good) Good: All subscales grade excellent or good Fair: Any one subscale grading fair

			• Radiographs (10 points) • Functional testing (10 points)		Poor: Any one subscale grading poor
Modified Cincinnati Rating Scale (MCRS)*	PRO	Disease specific	8 subscales: • Pain (20 points) • Giving way (20 points) • Swelling (10 points) • Walking ability (10 points) • Stair-walking (10 points) • Running (5 points) • Jumping/twisting (5 points) • Overall activity (10 points)	0–100	No interpretation of outcomes measure given
Stanmore Functional Rating System (SFRS)[21]	PRO	Disease specific	Levels of pain and activity • No pain • Slight pain with vigorous activity, ADL not affected • Mild pain after limited activity, ADLs tolerable • Moderate pain after limited activity, affecting ADLs • Severe pain with activity, pain with rest	0–4	Higher score = greater disability
Lysholm Knee Scoring Scale (LKSS) [16]	PRO	Disease specific	8 subscales (8 items): • Instability (30 points) • Pain (30 points) • Swelling (10 points) • Atrophy of thigh (5 points) • Stair climbing (10 points) • Squatting (5 points) • Limping (5 points) • Support (5 points)	0–100	Higher score = greater disability
Modified Lysholm Score (MLS)‡[20]	PRO	Disease specific	8 subscales (8 items): • Instability (25 points) • Pain (25 points) • Catching/locking (15 points) • Swelling (10 points) • Stair climbing (10 points) • Squatting (5 points) • Limping (5 points) • Support (5 points)	0–100	Excellent: 95–100 Good: 84–94 Fair: 65–83 Poor: <65
Tegner Activity Score (TAS)[20]	PRO		10 activity levels within 3 activities: • Competitive sports • Recreational sports • Work	0–10	Maximum 10: Competitive sports (national and international elite soccer) Minimum 0: Sick leave or disability pension
International Knee Documentation Committee (IKDS) Scale subjective	PRO	Disease specific	4 subscales (19 items): • Symptoms (44 points) • Sports activities (50 points) • Function (11 points)	0–100	Lower score = greater disability

knee form[22]					
International Cartilage Repair Society (ICRS) cartilage repair assessment[6, 7]	CBO	Disease specific	3 subscales (3 items) • Degree of defect repair (4 points) • Integration to border zone (4 points) • Macroscopic appearance (4 points)	0–12	Grade I Normal: 12 Grade II Nearly normal: 8–11 Grade III Abnormal: 4–7 Grade IV Severely abnormal: 1–3
International Cartilage Repair Society (ICRS) functional status[24]	PRO	Disease specific	4 levels: • Grade I – I can do everything I want with my joint • Grade II – I can do nearly everything that I want with my joint • Grade III – I am restricted and many things I want to do with my joint are not possible • Grade IV – I am very restricted and I can do almost nothing with my joint without severe pain and disability	Grade I–IV	Higher grade = greater disability
International Cartilage Repair Society (ICRS) activity level[24]	PRO	General health	4 levels • Grade I – High competitive sportsman/woman • Grade II – Well trained and frequently sporting • Grade III – Sporting sometimes • Grade IV – Non-sporting	Grade I–IV	Higher grade = greater disability
Modified/Hospital for Special Surgery Score (HSSS)†[11, 12]	CBO	Disease specific	7 subscales (12 items): • Pain (30 points) • Function (22 points) • Range of motion (18 points) • Muscle strength (10 points) • Deformity (10 points) • Instability (10 points) • Subtractions o Assistive device o Extension lag o Valgus/varus deformity Subtractions of 1-5 points for those items that apply.	0-100	Excellent: 85–100 Good: 70–84 Fair: 60–69 Poor: <60
Knee Injury Osteoarthritis Outcome Score (KOOS)[4]	CBO	Disease specific	5 subscales (42 items): • Pain (36 points) • Symptoms (28 points) • Activities of daily living (68 points) • Sports and recreation (20 points) • Quality of life (16 points)	Subscales scored separately 0-100	Lower score = greater disability
Marshall Knee Score[10]	CBO	Disease specific	3 subscales (22 items): • Subjective complaints (18 points) • Knee examination (12 points) • Stability (20 points)	0-50	Good -Excellent: 41–50 Fair (+): 36–40 Fair (-): 31–35 Poor: <30

Meyers Score[14]	CBO	Disease specific	3 subscales (3 items): • Pain (6 points) • Function (6 points) • Range of motion (6 points)	0-18	Excellent: 18 Good: 15–17 Fair: 12–14 Poor: <12
SF-36[25]	PRO	General health	8 subscales (36 items): • Physical functioning (10 items) • Mental health (5 items) • Bodily pain (2 items) • Physical role limitations (4 items) • General health (5 items) • Vitality (4 items) • Social functioning (2 items) • Emotional role limitations (4 items)	0-100	Lower score = greater disability
SF-12[26]	PRO	General health	2 subscales (12 items): Physical health • Physical functioning (2 items) • Physical role limitations (2 items) • Bodily pain (1 item) • General health (1 item) Mental health • Vitality/mental health (3 items) • Social functioning (1 item) • Emotional role limitations (2 items)	0-100	Lower score = greater disability
Pain Disability Index (PDI)[27]	PRO	Pain	7 subscales (7 items): • Family/home responsibilities • Recreation • Social activity • Occupation • Sexual behavior • Self-care • Life-support activity	0-70	Higher score = greater disability
EQ-5D[28]	PRO	General health	5 subscales (5 items): • Mobility • Self-care • Usual activity • Pain • Anxiety/depression	0-1 Preferential weights are assigned to each health state level to obtain a score of 0 (death) to 1 (optimal health).	Final score has a unique 5-digit descriptor, corresponding to the levels of disability of each category ranging from 11111 to 33333. Lower score = greater disability

*No reference given
†Study does not reference Outcome measure and refers to both modified HSSS and HSSS
‡Horas and Salzmann report a modification of the Lysholm used, but no additional reference given.

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Table F3. Demographics of studies validating outcomes measures in osteochondral patients.

Author (year)	Study design	Outcome measure evaluated	Follow-up (% followed)	Demographics	Patient characteristics	Interventions	Inclusion/Exclusion
Kocher (2004)	Prospective Cohort Study	Lysholm Knee Scale	% f/u: NR Length f/u*: -pre-op (Group B – 2 pre-ops) -3 months -6 months -12 months -yearly *Mean length or % of f/u: NR	Group A: (Total) N = 1657 Male: 61% (1011) Mean age: 44 (range, 14-88) years* Group B: (subset of A) N = 57 Male: 61% (35) Mean age: 44 (range, 28-64) years Group C: (subset of A) N = 248 Male: 67% (165) Mean age: 40 (range, 13-74) years* *Ranges don't match up (???)	Group A (1657): • Lysholm scale, demographic data, subjective assessment, and objective assessment • 679 (41%) with traumatic chondral injuries involving only 1 compartment o 230 ligament injuries o 285 meniscal injuries • 249 (15%) traumatic chondral injuires with 2 or more compartments o 65 ligament injuries o 107 meniscal injuries • 729 (44%) degenerative chondral lesions o 80 ligament injuries o 277 meniscal injuries Group B (57): • Arthroscopically documented chondral disorders • Lysholm scale, demographic data, subjective assessment, and objective assessment • 23 traumatic uni-compartmental chondral injuries o 15 isolated chondral lesions o 5 associated ligament injuries o 3 associated meniscal injuries • 9 traumatic chondral injuires with 2 or more compartments o 3 isolated chondral lesions o 5 associated ligament injuries o 1 associated meniscal injuries • 25 degenerative chondral lesions o 2 associated ligament injuries o 11 associated meniscal injuries	Test-Retest Reliability (Group B): • Patients completed original pre-op questionnaire and a second pre-op questionnaire within 4 weeks Internal Consistency (Group A): • Pre-op Lysholm scales Content Validity (Group A): • Pre-op Lysholm scales • Floor effects and ceiling effects were determined for the overall Lysholm scale and for the 8 domains Criterion Validity (Group C): • Pre-op Lysholm scales Construct Validity (Group A): • Pre-op Lysholm knee scales • 9 hypotheses (constructs) were developed by consensus and were tested Responsiveness (Group C): • Pre-op Lysholm knee scale scores were compared with the scores at a mean of 51.2 months (range, 12.5-79.4 months) after treatment with arthroscopic microfracture	Inclusion: -various chondral disorders of the knee Exclusion: NR

Author (year)	Study design	Outcome measure evaluated	Follow-up (% followed)	Demographics	Patient characteristics	Interventions	Inclusion/Exclusion
Kocher (2004) (Continued)					Group C (248): • Lysholm scale, SF-12, WOMAC, Tegner activity scale • 84 degenerative chondral lesions • 125 unicompartmental chon. lesions • 39 multicompartmental chon lesions • 107 isolated chondral defects • 66 associated ACL injury • 47 associated meniscal injury • 28 associated ACL and meniscal		

Author (year)	Study design	Outcome measure evaluated	Follow-up (% followed)	Demographics	Patient characteristics	Interventions	Inclusion/Exclusion
Briggs (2006)	Prospective Cohort Study	Lysholm Knee Score and Tegner Activity Scale	% f/u: NR Lysholm and Tegner measured at a minimum of 2 years post-op, and then again within 4 weeks Tegner score for internal consistency and content validity f/u: 42% (80/191)	**Test-retest reliability**: N = 122 Male: 63% (77) Mean age: 48 (range, 14-76) years **Internal consistency and content validity**: N = 191* Male: 68% (129) Mean age: 40 (range, 13-81) years *isolated meniscal lesion **Only 80 f/u with Tegner score Of the N = 80: Male: 63% (50) Mean age: 42 (range, 16-81) years N = 477* Male: 77% (367) Mean age: 39 (range, 18-62) years *meniscal lesion and associated intra-articular disease **Criterion**: N = 477 group **Construct validity**: N = 191 group **Responsiveness**: N = 668 (N = 191 group and N = 477 group)	N = 122 group: • Variety of arthroscopically documented meniscal disorders o 59 (48%) medial meniscus lesion o 40 (33%) lateral meniscus lesion o 23 (19%) medial and lateral meniscus lesion • 28 (23%) isolated meniscal lesion with no other ligament or chondral surface disorder N = 191 group: • Isolated meniscal lesion o 117 (61%) medial meniscus lesion o 60 (31%) lateral meniscus lesion o 14 (7%) medial and lateral meniscus lesion N = 80 subgroup: • Isolated meniscal lesion • Tegner score determined for this group (bc Tegner score was added to questionnaire after collection of the Lysholm score had already begun) o 42 (53%) medial meniscus lesion o 29 (36%) lateral meniscus lesion o 9 (11%) medial and lateral meniscus lesion N = 477 group: • Meniscal lesion and associated intra-articular disease o 120 patients had an ACL procedure performed o 261 patients had ≥ 1 previous operation (range, 1-8)	Test-Retest Reliability: • N=122 group • The Lysholm score and Tegner activity level were measured at a minimum of 2 years post-op and then again within the following 4 weeks Internal Consistency and Content Validity: • 2 groups: o N = 191 o N = 477 • The Lysholm score, Tegner activity level, demographic data, and patents' subjective assessments were recorded pre-op and at least one year post-op • Floor effects and ceiling effects were determined for the overall Lysholm score, for the eight domains of the Lysholm score, and for the Tegner activity scale Criterion Validity: • N = 477 group • Pre-op, these patients completed the SF-12 Health Survey in addition to the Lysholm score and Tegner activity scale questionnaires Construct Validity: • N = 191 group • Pre-op: 191 Lysholm scores and 80 Tegner activity scores as well • 8 hypotheses (constructs) were developed by consensus and tested in this group Responsiveness • N = 191 and N = 477 groups combined • Pre-op Lysholm and Tegner were compared with the scores at 12 months after treatment of the meniscal lesion	Inclusion: -meniscal injury of the knee Exclusion: NR

Author (year)	Study design	Outcome measure evaluated	Follow-up (% followed)	Demographics	Patient characteristics	Interventions	Inclusion/Exclusion
Smith (2009)	Prospective validation study of arthroscopic cartilage repair scores	International Cartilage Repair Society (ICRS) and Oswestry Arthroscopy Score (OAS)	100% f/u (6/6) 6 weeks f/u	5 arthroscopic surgeries Male: NR Mean age: NR	• 5 video clips of patients who had previously undergone autologous chondrocyte implantation (ACI) in the knee • Cases selected to represent a spectrum of macroscopic appearance, from good to poor	• 6 orthopaedic surgeons evaluated 5 arthroscopic video clips twice (6 weeks apart) o Each surgeon was asked to score the videos using both the ICRS and OAS systems o After 6 weeks, a second set of score forms was distributed to the panel of surgeons and the same videos were rescored • A questionnaire was also circulated to the scorers to make a subjective assessment of the face and content validity of the 2 systems • Validity (face and content): scorers filled out questionnaires • Reliability (equivalence and stability and inter-rater): scores were plotted against each other • Internal Consistency: looked at whether all items on a scale are correlated	Inclusion: NR Exclusion: NR

Author (year)	Study design	Outcome measure evaluated	Follow-up (% followed)	Demographics	Patient characteristics	Interventions	Inclusion/Exclusion
Bekkers (2009)	Retrospective questionnaire study	Knee Injury and Osteoarthritis Outcome Score (KOOS)	87% f/u (40/46) 2 day follow-up	N = 40 Male: 70% (28) Mean age: 35 ± 12 years (range, 18-55 years)	• All patients were treated for a symptomatic focal cartilage lesion o 50% (20) treated with autologous chondrocyte implantation o 50% (20) received microfracturing • Average post-op time: 32 months • 87% of patients had been treated between January 2005 and July 2006	• Patients received 2 sets of questionnaires (marked as Day 1 and Day 3) by mail, each containing the Dutch KOOS and complementary questionnaires (SF-36, Lysholm, EQ-5D) • Test-Retest Reliability: KOOS questionnaire with an interval of 2 days • Construct Validity: measured by comparing the subdomains of the KOOS with *a priori* hypothesized corresponding domains of the complementary questionnaires • Responsiveness: evaluated in another cohort of 36 patients of a recently published randomized trial comparing characterized chondrocyte implantation to microfracturing o Included patients completed the KOOS and the Marx activity rating scale (ARS) at baseline and 36 months follow-up o Standardized response mean (SRM) and effect size (ES) were calculated	Inclusion: • Patients treated for a focal cartilage lesion in the knee Exclusion: • Missing individual questionnaire items • Insufficient responses
van den Borne (2007)	Prospective cross-sectional study	ICRS and OAS	94% f/u (101/107)* *Images from 6 patients were missing, lost either during distribution and/or with problems in saving data to disk or network 4 weeks f/u	N = 101 images of arthroscopic procedures Male: NR Mean age: NR	• A total of 101 macroscopic images were evaluated o 52 cases of microfracture (21 prints and 31 videos) o 49 cases of ACI (16 prints and 33 videos) • 7 observers examined the images: o 4 orthopedic surgeons with extensive experience in cartilage surgery o 1 arthroscopy fellow o 1 orthopedic surgery resident o 1 clinical research manager with a non-medical background	• 7 observers judged 101 macroscopic images of cartilage repair (12 months after arthroscopic surgery), twice, with an interval of 4 weeks • Reliability: intra- and inter observer reliability were assessed by calculating the ICC for both measurement systems and for the estimated defect size • Validty: the Pearson correlation coefficient was used for testing equivalence correlation of both scoring systems and correlation between the mean estimated defect size	Inclusion: • Patients who underwent an arthroscopic procedure for cartilage repair (ACI or microfracture) Exclusion: NR

Author (year)	Study design	Outcome measure evaluated	Follow-up (% followed)	Demographics	Patient characteristics	Interventions	Inclusion/Exclusion
Smith (2005)		Lysholm Knee Scale	One time evaluation – no follow-up	N = 157 Male: 67% (107) Mean age: 37 ± 9.03 (range, 17-59) years	• 157 patients with isolated symptomatic cartilage defects: o 145 on the femoral condyle o 12 on the trochlea • Patients were from 18 different hospitals o 16 in the UK o 2 in Norway	• The Lysholm Knee Scale was completed by all 157 patients within 3 months prior to randomization and surgery • On the day patients completed the form, an independent assessor (a physiotherapist based at each hospital) carried out a semi-structured interview, a physical examination and functional tests with the patient • Based on information and observations from this assessment, and without looking at the patient's own scores, the assessor also completed the Lysholm Knee Scale. • Rasch analysis was used	Inclusion: • Patients with isolated symptomatic cartilage defects on the femoral condyle or trochlea • All patients had at least one previous procedure on the same defect which had failed to relieve symptoms Exclusion: • Patients with generalized osteoarthritis or knee instability

Author (year)	Study design	Outcome measure evaluated	Follow-up (% followed)	Demographics	Patient characteristics	Interventions	Inclusion/Exclusion
Greco (2010)	Prospective study with two cohort populations. LoE: II (as stated in the article)	International Knee Documentation Committee (IKDC) Subjective Knee Form compared to the following: WOMAC (Western Ontario And McMaster Universities Arthritis Index) Modified Cincinnati Knee Rating System Short Form 36	Baseline 6-month 12-month (final)	N = 136 Two subgroups: **Treatment cohort** n = 73 Male: Mean age: ± (range,) years **Stable cohort** n = 63 Male: Mean age: ± (range,) years	Treatment cohort: 73 patients with a primary diagnosis of an articular cartilage defect of the knee who were scheduled to undergo surgical intervention to repair the defect. Stable cohort 63 patients with a diagnosed articular cartilage dfect of the knee who had been treated with autologous chondrocyte implantation at least 5 years before this study.	• Surgical treatment in the treatment group included debridement, shaving, drilling, autologous chondrocyte implantation (ACI), abrasion arthroplasty, microfracture and cell therapy. • After informed consent, the 4 outcome instruments were randomly organized into booklets to avoid the effects that the order of presentation may have had on the results at baseline and each follow-up period • Patients were also asked a global rating of change question at the 6 and 12-month follow up and this measure was used to compare to the 4 outcome instruments for levels of responsiveness. • The surgeon completed orthopaedic history and recording data from the examination using the IKDC Knee History and Knee Examination forms. The history and examination data were used only to confirm eligibility and for descriptive purposes. No attempt was made to combine the history and examination data with the IKDC Subjective Knee Form to determine an overall IKDC rating. • The stable cohort-eligible patients were mailed a packet explaining the study with a consent form, demographic form and the 4 patient-reported outcome measures. • To assess whether the condition of the patients' knees would remain stable during the 12-month follow-up patients were then excluded from the study if their modified Cincinnati Score was less than 5, their modified Cincinnati Score changed more than 2 points since their rating 5 years after ACI, or they reported an additional knee injury, surgery, or failed ACI during the time after their 5-year registry evaluation. • Patients meeting the baseline criteria were mailed the 4 pateient-reported outcome instruments and the global rating of change question at 6 and 12 months.	Treatment cohort: • Patients having at least 1 symptomatic full-thickness (Outerbridge grade III or IV) chondral lesion of the femoral condyle or trochlea requiring surgical treatment and if they had a grade II or less cartilage lesion on the tibia and patella. • Exclusion criteria for the treatment group included: • Widespread arthritis in the involved joint, • History of total meniscectomy in the involved compartment of the knee, • Required treatment of both knees, • Had a bipolar defect in which there were opposing lesions on the femur and tibia, • Concurrent total meniscectomy or meniscal allograft in the involved knee. Stable cohort: • Met the same criteria as stated for the treatment cohort before ACI surgery. Potential patients for the stable cohort were excluded if they had had the ACI procedure on both knees, failure, revision or a procedure that violated the subchondral bone to treat the defect.

Table F4. Results of studies validating outcomes measures in osteochondral patients.

Author (year)	Instrument	Validity	Reliability	Responsiveness	Floor ceiling effect	MCID

Author (year)	Instrument	Validity	Reliability	Responsiveness	Floor ceiling effect	MCID
Kocher (2004)	Lysholm Knee Scale (LKS)	Content: • Overall mean score on LKS was 58.3 ± 19.0 (range, 2 to 100) with acceptable (<30%) floor and ceiling effects • Domains of pain, swelling, limp, instability, support, stair-climbing, and locking had acceptable (<30%) floor effects • Domains of pain, swelling, squatting, and stair-climbing demonstrated acceptable ceiling effects (<30%) • Domain of squatting had a high (>30%) floor effect • Domains of limp, instability, support, and locking had high (>30%) ceiling effects Criterion: • SF-12: Physical functioning, role physical and bodily pain domains ($p < .05$) • WOMAC: Pain, stiffness, function domains ($p < 0.05$) • Tegner Activity Scale ($p < .05$) Construct: • Patients with lower activity levels had lower scores ($r = .410$, $p < .001$) • Patients with greater number of chondral surfaces with Outerbridge grade-4 changes had lower scores ($p < .001$) • Patients with full thickness chondral defects had lower scores than patients with partial thickness chondral defects ($p = .001$) • Patients with chondral defects and associated meniscal tears had lower scores than patients with isolated chondral defects ($p = .01$) • Patients who had more difficulty with ADLs had lower scores than patients with less difficulty with ADLs ($r = .421$, $p < .001$) • Patients with more difficulty working because of knee had lower scores than those with less difficulty working ($r = .407$, $p < .001$) • Patients with more difficulty with sports because of knee had lower scores than patients with less difficulty with sports ($r = .330$, $p < .001$) • Patients with previous knee surgery had lower scores than patients without previous knee surgery ($p = .001$) • Patients with a poorer assessment of overall knee function had lower scores than patients with better assessment of overall knee function ($r = .475$, $p < .001$)	Internal consistency: • Overall LKS: $\alpha = .65$ Reproducibility: • Overall LKS: ICC = .91 (.82-.98) • Pain: ICC = .61 (.50-.77) • Instability: ICC = .82 (.73-.91) • Locking: ICC = .97 (.90-.99) • Stair-climbing: ICC .67 (.53-.83) • Limp: ICC = .82 (.71-.92) • Support: ICC = .98 (.91-1.00) • Swelling: ICC = 0.94 (.85-.99) • Squatting: ICC = .91 (.82-.98)	Effect size: • Overall LKS: 1.16 • Pain: 1.31 • Swelling: 1.17 • Limp: 1.29 • Squatting: 1.25 • Instability: .21 • Support: .59 • Stair-climbing: .75 • Locking: .55 Standardized response mean: • Overall LKS: 1.10 • Pain: 1.28 • Swelling: .20 • Limp: .50 • Squatting: .70 • Instability: 1.27 • Support: .54 • Stair-climbing: 1.08 • Locking: 1.24	Floor effect: • Overall LKS: 0 (0%) • Pain: 430 (26%) • Swelling: 201 (12.1%) • Limp: 145 (8.8%) • Squatting: 859 (51.8%) • Instability: 83 (5%) • Support: 226 (13.6%) • Stair-climbing: 323 (19.5%) • Locking: 16 (1%) Ceiling effect: • Overall LKS: 12 (0.7%) • Pain: 74 (4.5%) • Swelling: 318 (19.2%) • Limp: 537 (32.4%) • Squatting: 99 (6%) • Instability: 1104 (66.6%) • Support: 914 (55.2%) • Stair-climbing: 211 (12.7%) • Locking: 1023 (61.7%)	NR

Author (year)	Instrument	Validity	Reliability	Responsiveness	Floor ceiling effect	MCID
Briggs* (2006)	Lysholm Knee Scale (LKS)	Content: • Overall mean score on LKS was 61.7 ± 20.4 (range, 6 to 100) in group with both meniscal lesion and associated intra-articular lesion Criterion: NR Construct: NR	Internal consistency: • Overall LKS: α = .729 Reproducibility: NR	NR	NR	NR
	Tegner Activity Scale (TAS)	Content: • Overall mean score on TAS was 3 ± 1.7 (range, 0 to 10) in group with both meniscal lesion and associated intra-articular lesion Criterion: NR Construct: NR	Internal consistency: NR Reproducibility: NR	NR	NR	NR
Smith (2009)	Lysholm Knee Scale (LKS)†	Content: NR Criterion: NR Construct: • Rasch model [mean item fit -.26, standard deviation (SD) 1.01]	Internal consistency: • Remained adequate for group use with a person separation index (PSI) of .73 Reproducibility: • Overall LKS: ICC = .9 (.86-.93) • Bland-Altman plot showed no consistent difference in ratings	NR	NR	NR

Author (year)	Instrument	Validity	Reliability	Responsiveness	Floor ceiling effect	MCID
Bekkers (2009)	Knee Injury Osteoarthritis Outcome Score (KOOS)	Content: NR Criterion: NR Construct: Spearman's Rank correlation: • Symptoms (SF-36 Physical Functioning): rs = .585, p < .001 • Pain (SF-36 Pain): rs = .661, p < .001 • Function ADL (SF-36 Physical Functioning): rs = .558, p < .001 • Sport/recreation (Lysholm: rs = .700, p < .001 • QoL (EQ-5D): rs = .43, p = .006	Internal consistency: • Overall KOOS: α = .96 • Symptoms: α = .74 • Pain: α = .88 • Function ADL: α = .95 • Sport/recreation: α = .89 • QoL: α = .90 Reproducibility: ICC • Overall KOOS: ICC = .97 (.93-.98) • Symptoms: ICC = .95 (.90-.97) • Pain: ICC = .92 (.86-.96) • Function ADL: ICC = .87 (.77-.93) • Sport/recreation: ICC = .89 (.81-.93) • QoL: ICC = .95 (.91-.97) Smallest detectable difference (SDD) • Overall KOOS: SDD = 4 • Symptoms: SDD = 5 • Pain: SDD = 6 • Function ADL: SDD = 7 • Sport/recreation: SDD = 12 • QoL: SDD = 7	Effect size (ES) – mean change in score from baseline to 36 months f/u divided by SD of preop score ES: • Overall KOOS: .91 • Symptoms: .72 • Pain: .82 • Functional ADL: .70 • Sport/recreation: .98 • QoL: 1.32 Standardized response mean (SRM) – indicates mean change in score from baseline to 36 months f/u divided by the SD of mean change SRM: • Overall KOOS: .85 • Symptoms: .61 • Pain: .71 • Functional ADL: .75 • Sport/recreation: .87 • QoL: .76	Floor effect: • Overall KOOS: 0% • Symptoms: 0% • Pain: 0% • Functional ADL: 0% • Sport/recreation: 0% • QoL: 0% Ceiling effect: • Overall KOOS: 2.6% • Symptoms: 2.6% • Pain: 5.1% • Functional ADL: 7.7% • Sport/recreation: 7.7% • QoL: 10.3%	NR

Author (year)	Instrument	Validity	Reliability	Responsiveness	Floor ceiling effect	MCID
Greco (2010)	International Knee Documentation Committee (IKDC) Subjective Knee Form	Content: NR Criterion: NR Construct: NR	Internal consistency: NR Reproducibility: ICC • Overall IKDC at 6 months: ICC = .91 (.76-.97) • Overall IKDC at 12 months: ICC = .93 (.82-.98) Standard Error of Measurement – SEM • Overall IKDC at 6 months: SEM = 5.6 • Overall IKDC at 12 months: SEM = 4.9 Minimal Detectable Change – MCD • Overall IKDC at 6 months: MCD = 15.6 • Overall IKDC at 12 months: MCD = 13.7	6 months: Change scores: 11.5 ± 20.4 ES: .76 SRM: .57 12 months: Change scores: 19.4 ± 19.2 ES: 1.06 SRM: 1.00	Floor effect: NR Ceiling effect: No ceiling effect experienced	MCID at 6 months: 6.3 MCID at 12 months: 16.7

Author (year)	Instrument	Validity	Reliability	Responsiveness	Floor ceiling effect	MCID
	Modified Cincinnati Rating Scale (MCRS)	Content: NR Criterion: NR Construct: NR	Internal consistency: NR Reproducibility: ICC • Overall MCRS at 6 months: ICC = .91 (.77-.97) • Overall MCRS at 12 months: ICC = .80 (.48-.93) Standard Error of Measurement – SEM • Overall MCRS at 6 months: SEM = 5.5 • Overall MCRS at 12 months: SEM = 8.2 Minimal Detectable Change – MCD • Overall MCRS at 6 months: MCD = 15.3 • Overall MCRS at 12 months: MCD = 22.8	6 months: Change scores: 13.1 ± 25.4 ES: .6 SRM: .52 12 months: Change scores: 21.7 ± 28.6 ES: 1.09 SRM: .76	Floor effect: NR Ceiling effect: Ceiling effect experienced	MCID at 6 months: 14.0 MCID at 12 months: 26.0

Author (year)	Instrument	Validity	Reliability	Responsiveness	Floor ceiling effect	MCID
van den Borne (2007)	International Cartilage Repair Society (ICRS) cartilage repair assessment	Content: NR Criterion: NR Construct: Pearson correlation coefficient: • Oswestry Arthroscopy Score (OAS)‡: .94	Internal consistency: • Overall ICRS: α = .79 Reproducibility: Whole group: • Intraobserver: .73 (SD .05) • Interobserver: o 1st eval = .62 o 2nd eval = .61 Experienced observer group: • Intraobserver: .70 (SD .04) • Interobserver: o 1st eval = .62 o 2nd eval = .61 Good quality group: • Intraobserver: .74 (SD .11) • Interobserver: o 1st eval = .66 o 2nd eval = .69	NR	NR	NR
Smith (2005)	International Cartilage Repair Society (ICRS) cartilage repair assessment	Content: Questionnaire given to a panel of scorers to assess whether test appears to be reasonable way of gaining information. All, but one scorer agreed that ICRS was a reasonable method of assessing articular cartilage repair. ICRS gives no allowance for hypertrophy of a grafted area, therefore one could expect a hypertrophied graft to score better. Criterion: NR Construct: Pearson correlation coefficient: • Oswestry Arthroscopy Score (OAS)‡: .88 (range, .76-.94), (p < .01)	Internal consistency: • Overall ICRS: α = .91 Reproducibility: ICC • Overall ICRS test-retest: ICC = .94 • Overall ICRS intra-rater: ICC: = .83	NR	NR	NR

*Only population that had combined meniscal lesion and intra-articular lesion used in psychometric analysis
†Removed the item swelling from the original scale
‡ICRS and OAS both correlated well with each other and are both reliable. However, OAS may score slightly better. OAS found to be both valid and reliable in osteochondral population, but not used in comparative studies.

Table F5. Demographics and results of studies assessing the reliability of knee articular cartilage classification in osteochondral patients.

Author (year)	LoE	Study conditions	Reliability/ classification assessed	Patient demographics	Results
Marx (2005)	III	Videotaped knee arthroscopies N = 31 lesions with grade 2 and 3 lesions combined n = 20 ACL reconstructions; n = 11 additional patients with more significant articular cartilage damage N = 22 lesions without grade 2 and 3 lesions combined 6 experienced orthopedic surgeons from 5 centers analyzed the videos No mention of blinding between raters or of raters to the clinical results	Inter-rater reliability Lesion severity: Modified Outerbridge Classification	NR	**Inter-rater agreement for lesion with grade 2 and grade 3 lesions combined (n = 31)** Location / Expected agreement, % / Observed agreement, % / Kappa Lateral articular lesions Femoral condyle: 0.55 / 0.94 / 0.86 Tibial plateau: 0.61 / 0.81 / 0.51 Patellar: 0.58 / 0.93 / 0.80 Trochlear: 0.67 / 0.90 / 0.71 Medial articular lesions Femoral condyle: 0.56 / 0.93 / 0.84 Tibial plateau: 0.79 / 0.87 / 0.34 Patellar: 0.56 / 0.94 / 0.87 Trochlear: 0.67 / 0.92 / 0.76 **Inter-rater agreement for lesion without grade 2 and grade 3 lesions combined (n = 22)** Cartilage grade / Expected agreement, % / Observed agreement, % / Kappa 1: 0.5 / 3.4 / 0.45 2: 13.2 / 22.3 / 0.41 3: 24.9 / 38.1 / 0.52 4: 0.4 / 3.4 / 0.52 Overall: 38.9 / 67.2 / 0.47
Niemeyer (2011)	III	Comparison of arthroscopic vs. open assessment (gold standard) N = 450 focal cartilage defects in 407 patients who underwent ACI Unclear to what extent raters were blinded Subanalyses conducted based on surgeon experience (i.e. number of knee arthroscopies performed): Inexperienced (< 100) Experienced (100-1000) Expert (> 1000)	Inter-rater reliability Lesion size: Small (≤ 4 cm^2) Medium (> 4 cm^2 but < 6 cm^2) Large (≥ 6 cm^2) Lesion severity: ICRS classification	Mean age: 35.7 ± 9.2 years Lesion location: Medial femoral condyle: n = 195 Lateral femoral condyle: n = 38 Patella: n = 158 Trochlea: n = 59	**Lesion size** Mean defect size, arthroscopic vs. open: 5.69 ± 1.81 vs. 4.54 ± 2.11; *P* < .001; Number of lesions (%) / Mean over or under estimation (cm^2) / Direction / P-value for comparison between defect sizes Small: 233 (51.8) / 1.64 ± 1.05 / Over / < .01 Medium: 171 (38.0) / 0.91 ± 1.15 / Over / < .01 Large: 46 (10.2) / -0.36 ± 2.22 / Under / < .01 In inexperienced surgeons, a significant trend toward overestimating defect size was found compared with experienced (P = .006) and expert (P < .001) surgeons. **Lesion severity** Lesion location / Number of lesions (%) / Correctly classified (vs. open evaluation); n (%) / Underestimate 1 grade / Overestimate 1 grade / Overestimate 2 grades Medial femoral condyle: 195 (43.3) / 161 (82.6) / 7 / 26 / 1

Author (year)	LoE	Study conditions	Reliability/ classification assessed	Patient demographics	Results
					Lateral femoral condyle 38 (.08) 28 (73.7) 5 5 0 Patella 158 (35.1) 132 (83.5) 16 10 0 Trochlea 59 (13.1) 44 (74.6) 7 8 0
Spahn (2011)	II	Arthroscopically assessed 14 cartilage areas per patient (n = 224) 4 experienced surgeons Documentation of grade was done anonymously and raters were blinded to each other's grading	Inter-rater reliability Lesion severity: ICRS classification	N = 16 Male: 56.3% Mean age 45.3 ± 14.9 years Complained knee pain for a mean 6.9 ± 4.5 months No history of prior surgery or trauma None received OAT/ mosaicplasty (autograft or allograft)	**Agreement between clinicians** **n (%)** Complete agreement (all 4) 39 (17.4) Agreement between 3 84 (37.5) Agreement between 2 101 (45.1) Difference of 1 grade 101 (46.9) Difference of 2 grades 39 (17.4) Difference of 3 grades 41 (18.3) **Cohen (Fleiss) Kappa Index for multiple investigators by anatomic region** Region evaluated — Kappa Femoral condyles Medial (mean bearing zone) 0.193 Medial margin 0.116 Lateral (mean bearing zone) 0.309 Lateral margin 0.111 Tibial Plateau Medial (mean bearing zone) 0.168 Medial margin 0.164 Lateral (mean bearing zone) 0.020 Lateral margin 0.085 Patella Medial 0.052 Central 0.300 Lateral 0.170 Trochlea Medial 0.292 Central 0.255 Lateral 0.234

ACI: autologous chondrocyte implantation: ACL: anterior cruciate ligament; ICRS: International Cartilage Repair Society; LoE: level of evidence; NR: not reported.

Appendix G. RCTs – Data Abstraction

The first set of tables describes the study design and patient population. The second set of tables provide results

DEMOGRAPHIC AND STUDY DETAIL

Table G1: Characteristics of RCTs comparing OATS/mosaicplasty with other interventions in the knee

<table>
<tr><th>Author (year)</th><th>Study design (LoE) Funding</th><th>Study period Follow-up (% followed)</th><th>Patient Characteristics</th><th>Inclusion, exclusion</th><th>Defect/Lesion Characteristics</th><th>Interventions and co-interventions</th><th>Outcomes</th></tr>
<tr><td colspan="8">Mosiacplasty versus autologous chondrocyte implantation (ACI)</td></tr>
<tr><td colspan="8">Knee</td></tr>
<tr>
<td>Bentley (2003)</td>
<td>RCT

LoE: IIb

<u>Funding</u>:
Authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this study.</td>
<td>Mean F/U: 19 (12 – 31) months
F/U rate 100%</td>
<td>N = 100 (100 knees)
57% male
Mean age: 31.3 (range, 16 – 49) years

<u>Mosaicplasty</u>
n = 42
Sex: NR
Mean age: 31.6 (range, 20 – 48) years

<u>ACI</u>
n = 58
Sex: NR
Mean age: 30.9 (range, 16 – 49) years

<u>Patient characteristics</u>
Previous surgery: 94%
• Of these, all had undergone arthroscopy, and the mean number of additional operations was 1.5 (0–4).</td>
<td><u>Inclusion:</u>
Consecutive patients with symptomatic lesions of the articular cartilage of the knee. Primary indication for surgery: persistent pain, reduction in activities. Other symptoms included giving way, catching, locking, and swelling of the knee.

<u>Exclusion:</u>
NR</td>
<td>Etiology
<table>
<tr><th></th><th>Total</th><th>ACI</th><th>Mosaic</th></tr>
<tr><td>Trauma</td><td>46/100</td><td>24/58</td><td>22/42</td></tr>
<tr><td>OCD</td><td>19/100</td><td>14/58</td><td>5/42</td></tr>
<tr><td>CMP</td><td>14/100</td><td>12/58</td><td>2/42</td></tr>
<tr><td>Other</td><td>21/100</td><td>8/58</td><td>13/42</td></tr>
<tr><td colspan="4">Anatomical distribution</td></tr>
<tr><td>MFC</td><td>53/100</td><td>24/58</td><td>29/42</td></tr>
<tr><td>Patella</td><td>25/100</td><td>20/58</td><td>5/42</td></tr>
<tr><td>LFC</td><td>18/100</td><td>13/58</td><td>5/42</td></tr>
<tr><td>Trochlea</td><td>3/100</td><td>1/58</td><td>2/42</td></tr>
<tr><td>LTC</td><td>1/100</td><td>0/58</td><td>1/42</td></tr>
<tr><td colspan="4">Size (mean): 4.6 (1–12.2) cm²</td></tr>
<tr><td colspan="4">Location: 61 right; 39 left</td></tr>
</table>
</td>
<td>Arthroscopy carried out on all patients prior to randomization to determine suitability for cartilage grafting (i.e., osteochondral or condral defect > 1 cm in diameter in a joint which was otherwise biomechanically normal and free of inflammatory disease).

<u>Mosaicplasty</u> (one-stage procedure)
• Open procedure
• Residual cartilage remnants removed
• Autograft source site: margins of trochlea (preferred) or margins of intercondylar notch
• Mosaic plug diameter: 4.5 mm (when possible)
• Slope of the donor articular surface matched to that of the recipient site</td>
<td>• Function (Modified Cincinnati, Rating System, Stanmore Functional Rating System)
• Second look arthroscopy (and biopsy in ACI patients) when possible (1 year)
• Reoperation
• Infection
• DVT

Grading of functional results:
• Excellent: > 80
• Good: 55–79
• Fair: 30–45
• Poor: < 30

Clinical correlations to scores:
• Improved: excellent or good (ie., ≥ 55)
• Unchanged: fair (30–45)</td>
</tr>
</table>

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
			Duration of symptoms: mean 7.2 years (range NR) Comorbidities: NR Classification: NR Co-existing abnormalities: NR			• Plugs placed slightly prominently to allow contact with opposing articular surface during normal movement. • Normal ROM and stability of plugs verified prior to closure. • Prophylactic antibiotics at time of surgery and at 6 and 12 hours postop • Wound closed with absorbable sutures, steristrips, and drainage **ACI** (two-stage procedure) First stage • Arthroscopy • Harvesting of full-thickness articular cartilage (approx. 2 x 1 cm) from trochlea margin ACI preparation • Cartilage digested enzymatically to release cells • Cell culture done in patient's serum (taken during surgery) Second stage (3-5 weeks later) • Open arthrotomy • Residual cartilage remnants removed • Defect covered by piece of porcine collagen OR periosteum taken from patient's tibia or femur, which was sutured in place and sealed with fibrin glue • Cultured ACI cells (mean 5.5 (5–10) million cells) delivered behind	• Worse: poor (< 30)

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
						membrane with syringe and fine catheter; filled to infation of membrane without overflow or excess pressure • Prophylactic antibiotics at time of surgery and at 6 and 12 hours postop • Wound closed in layers with non-absorabable sutures and without drainage **Co-interventions** • Rehab identical for both techniques • No early movement of knee allowed prior to 24 hours • Full weight-bearing with crutches at 24 hours • Light cylinder cast with knee in full extension at 48 hours; removed at 10 days • Crutches required for 6 weeks • Daily physiotherapy for two weeks, after which other activities encouraged as long as impact loading and twisting strains on knee avoided • Patients returned to normal activities of daily living and work at 6 weeks; physiotherapy continued if necessary • Light jogging allowed at 6 months; sporting activity allowed at 12 months	

<table>
<tr><th>Author (year)</th><th>Study design (LoE) Funding</th><th>Study period Follow-up (% followed)</th><th>Patient Characteristics</th><th>Inclusion, exclusion</th><th>Defect/Lesion Characteristics</th><th>Interventions and co-interventions</th><th>Outcomes</th></tr>
<tr>
<td>Horas (2003)</td>
<td>Quasi-RCT

LoE: IIb

Funding: No benefits received or will be received from a commercial party related directly or indirectly to the subject of this study.</td>
<td>F/U: 24 months

F/U rate: NR</td>
<td>N = 40 patients (40 knees)
58% male
Mean age: 33.4 (range, 18–44) years

<u>OATS</u>
n = 20
75% male
Mean age: 35.4 (range, 21–44) years
Average weight: 80 (range, 54 – 96) kg
Average height: 180 (range, 164 – 192) cm

<u>ACI</u>
n = 20
40% male
Mean age: 31.4 (range, 18–42) years
Average weight: 71 (range, 52 – 86) kg
Average height: 175 (range, 162 – 186) cm

Previous surgery: 28%: ACI (7/20), OATS (4/20)
• Prior surgical abrasion arthroplasty: 9/40; ACI (7/20), OATS (2/20)
• Prior drilling of cartilage defect: 2/40; ACI (0/20), OATS (2/20)

Comorbidities: NR

Classification: NR

Co-existing abnormalities: NR</td>
<td><u>Inclusion</u>:
• History of single traumatic event
• Single cartilage lesion extending to or through the articular cartilage tidemark without an osseous lesion
• Location of lesion in weight-bearing area of femoral condyle
• Age 18 – 45 years
• Clinical symptoms such as locking, pain with weight-bearing, swelling

<u>Exclusion</u>:
• Knee joint instability
• Matching lesion on opposing tibial articular surface
• Axial malalignment (>10° of varus or valgus)
• Osteochondral tumor
• Skeletal immaturity
• Degenerative or rheumatoid joint disease
• Refusal by patient to be randomly assigned to treatment group</td>
<td>Anatomical distribution
<table>
<tr><th></th><th>Total</th><th>ACI</th><th>OATS</th></tr>
<tr><td>MFC</td><td>33/40</td><td>17/20</td><td>16/20</td></tr>
<tr><td>LFC</td><td>7/40</td><td>3/20</td><td>4/20</td></tr>
<tr><td colspan="4">Size (cm²) (range 3.2 to 5.6)</td></tr>
<tr><td></td><td>3.75</td><td>3.86</td><td>3.63</td></tr>
</table>
</td>
<td><u>ACI</u> (two-stage procedure)
First stage
• Arthroscopy
• Harvesting of articular cartilage (140–360 mg) from proximal MFC
ACI preparation
• 2-3 weeks duration
Second stage (2-3 weeks later)
• Medial or lateral open arthrotomy
• Injured cartilage excised until going into completely healthy hyaline cartilage down the subchondral bone plate and avoiding bleeding of the site
• Defect covered with exact fitting periosteal flap taken from the medial aspect of the proximal part of the tibia, sutured to the hyaline cartilage surrounding the defect (fibrin glue not used). Watertight seal confirmed.
• Cultured ACI cells (3.2–6.5 x 10^6) delivered behind membrane, injection site closed with final suture
• Wound closed in layers (details NR)

<u>OATS</u> (one-stage procedure)
• Open procedure
• Autograft harvesting site NR
• Autografts harvested using diamond bone</td>
<td>• Modified Lysholm score
• Meyers score
• Tegner activity scale
• Second-look arthroplasty and biopsy (for histological analysis) if patient consented</td>
</tr>
</table>

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
						cutting system with carving cylinder 0.1 cm larger than that used to carve out the lesion • Resurfacing area could range from 0.78–2.26 cm² with the available cylinders • Press-fit implantation without additional fixation • If defects required multiple cylinders (ie., large defects or in order to maintain joint congruency), press-fit implantation of several single osteochondral transplants were used • Number of cylinders/patient: mean 1.8 (range, 1–3) **Co-interventions** • Rehab identical for both techniques • Brace not used • Non-weight bearing with crutches for first 14 days; weight bearing gradually increased to full-weight bearing by 12 weeks • Limited range of motion 0° to 90° (varied by patient) first 10 days, gradually increased to full range of motion at 12 weeks • Active and passive physiotherapy began at 4 weeks and continued to 12 weeks. Full activity allowed after 12 weeks, recommended to permanently refrain from	

<table>
<tr><th>Author (year)</th><th>Study design (LoE) Funding</th><th>Study period Follow-up (% followed)</th><th>Patient Characteristics</th><th>Inclusion, exclusion</th><th>Defect/Lesion Characteristics</th><th>Interventions and co-interventions</th><th>Outcomes</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td>participating in competitive contact sports (e.g., soccer, baseball, hockey)</td><td></td></tr>
<tr><td>Dozin (2005)</td><td>RCT

LoE: IIb

Funding: NR</td><td>Mean F/U: 296 (range, 0 to 1339) days

Mean F/U ACI group: 291 (range, 0 to 1339) days

Mean F/U Mosaicplasty group: 300</td><td>N = 44 (only 23/44 received mosaicplasty or ACI)*
61.4% male
Age: 28.7 ± 7.71
Weight: 71.5 kg ± 13
Height: 173 cm ± 9.5

Mosaicplasty n = 22 (11/22 underwent mosaicplasty)*</td><td><u>Inclusion</u>:
• Age of 16 to 40 years
• Cartilaginous lesion presenting a focal symptomatic chondral injury of III° or IV° Outerbridge grade without subchondral bone</td><td>Anatomical distribution
<table><tr><th></th><th>Total</th><th>ACI</th><th>Mosaic</th></tr><tr><td>MFC</td><td>26/44</td><td>14/22</td><td>12/22</td></tr><tr><td>LFC</td><td>5/44</td><td>2/22</td><td>3/22</td></tr><tr><td>Patella</td><td>13/44</td><td>6/22</td><td>7/22</td></tr><tr><td>Size (cm)</td><td></td><td></td><td></td></tr><tr><td></td><td>1.925 ± 0.63</td><td>1.97 ± 0.43</td><td>1.88 ± 0.45</td></tr><tr><td>Outerbridge Grade</td><td></td><td></td><td></td></tr><tr><td>III°</td><td>10/44</td><td>6/22</td><td>4/22</td></tr><tr><td>IV°</td><td>34/44</td><td>16/22</td><td>18/22</td></tr></table></td><td><u>ACI</u>
• Medial or lateral open parapetellar arthrotomy performed
• Chondral lesion debrided down to best cartilage available
• Autograft consisted of periosteal flap taken from proximal medial subcutaneous tibia and</td><td>• Lysholm knee scoring scale
• International knee documentation committee scale</td></tr>
</table>

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
		(range, 0 to 994) days Precise f/u rate cannot be determined – number eligible not reported. F/U rate ater randomization 52%*	45.5% male Age: 27.9 ± 8.08 Weight: 70 kg ± 14 Height: 170 cm ± 7 BMI <20: 1/6 (6.3%) BMI 20-25: 13/16 (81.3%) BMI 25-30: 2/16 (12.5%) <u>ACI</u> n = 22 (12/22 underwent ACI)* 77.3% male Age: 29.6 ± 7.31 Weight: 73 kg ± 12 Height: 176 cm ± 10 BMI <20: 2/18 (11.1%) BMI 20-25: 11/18 (61.1%) BMI 25-30: 5/18 (27.8%) Comorbidities: NR Classification: Outerbridge Co-existing abnormalities: NR	injury or loss • History of single traumatic event or microtraumatic (repetitive low impact injury) cause • Symptoms characterized by episodes of pain and/or swelling and/or pseudolocking • Location of lesion in weight-bearing area of femoral condyle or patella • Lesion dimension of at least 1 cm diameter • No previous surgical treatment of the lesion of interest <u>Exclusion</u>: • Overweight • Associated injury to or loss of subchondral bone • Knee joint instability • Associated meniscal damage or injured anterior cruciate ligament • Axial misalignment • Rheumatoid joint disease • Previous or current neoplasy • HIV, HBV, or HCV viral infection		sutured to surrounding rim of debrided cartilage • Periosteal rim sealed with fibrin glue except one corner where the expanded chondrocytes injected into defect • This corner closed with final suture and application of fibrin sealant **<u>MOS</u>** • Open procedure • All fibrous tissue was excised down to a base of cancellous bone that was abraded to viable subchondral bone to expose a bleeding floor that would promote fibrocartilage ingrowth between the grafts after transplantation • Recipient holes (approximately 15 mm deep) were made perpendicular to the chondral surface • Laser marks on drill bits used to determine depths • Specially designed drill guide was used to keep recipient holes separated by 1 mm bone • Autograft taken from periphery of the femur or the notch area, with the patellar groove preserved • Small 15-mm sagittal incison just medial or lateral to patellar edge made and specially designed tubular chisels used to harvest each graft	

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
						• Using a smooth cannula, the graft was delievered into each recipient hole **Co-interventions** • Rehab identical for both techniques • No knee brace used • Non-weight bearing or foot-touch weight bearing with crutches for first 4 weeks • From 4th to 5th week, weight-bearing was increased • Active and passive physical therapy was begun immediately • Continuous self-assisted passive motion was started 2nd day post-surgery to promote joint nutrition and prevent adhesions • Range of motion limited to 0° to 90° during first 2 weeks and gradually increased thereafter • At 4 weeks isometrics, proprioceptive exercises, and muscular strengthening prescribed and progressively increased • Return to sports involving cutting and contact sports were not to be attempted until 6 months post-surgery	
OATS/mosaicplasty vs. microfracture							
Gudas (2005)	RCT LoE: IIb	Mean F/U: 37.1 (range, 36 to 38) months F/U rate 95%	N = 60 athletes (60 knees) Age: 24.3	Inclusion: • Articular cartilage defects of medial or lateral condyle	**Etiology** Trauma: Total 32/57; MF 17/29; OATS 15/28	Arthroscopy carried out on all patients to determine suitability for study and patients randomized to MF	• International Cartilage Repair Society (ICRS) cartilage-injury grading system

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
	Funding: NR	• 3 patients (2 OATS, 1 MF) did not return for evaluation	OATS n = 28 Sex: NR Age: NR Microfracure n = 29 Sex: NR Age: NR Duration of symptoms: 21.32 ± 5.57 months Previous surgery: 0/60 Comorbidities: NR Classification: International Cartilage Repair Society (ICRS) cartilage-injury grading system used to classify defects. Co-existing abnormalities: NR	• Articular cartilage defects between 1 and 4 cm² • Competitive or well-trained athletes before injury (according to ICRS) • Age < 40 years Exclusion: • Lesions > 4 cm² • Ligament-deficient knees	OCD: 25/57; 12/29; 13/28 **Size** (cm²) Mean: 2.77 ±.68; 2.80 ±.65 1-2 cm²: 14/57; 8/29; 6/28 2-3 cm²: 25/57; 12/29; 13/28 3-4 cm²: 18/57; 9/29; 9/28 **Anatomical distribution on femoral condyle** Anterior: 12/57; 7/29; 5/28 Central: 33/57; 17/29; 16/28 Posterior: 12/57; 5/29; 7/28	or OATS procedure **MF** • Arthroscopic • Exposed bone was debrided of all the remaining unstable cartilage • Calcified cartilage layer was always removed • Awl used to make multiple holes or microfracures in subchondral bone in the exposed subchondral bone plate • Holes were made as close together as possible, taking care not to break into another and thus damage subchondral plate between them • Holes approximately 2 to 4 mm wide and as close as possible to each other **OATS** • Arthroscopic • Remnants of residual cartilage and calcified layers of subchondral bone were removed from the defect • Autografts harvested were 5.5 mm diameter plugs from lateral and/or medial margin of the femoral trochlea • Donor transplant was harvested with a larger (0.1-mm) cylinder, and lesion was carved out with a smaller cylinder, so press-fit transplantation of the osteochondral cylinder	• Hospital for Special Surgery (HSS) score • Donor-site morbidity • Infection

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
						could be achieved • Average of 4.3 osteochondral plugs (range, 3 to 6 plugs) used • Prophylactic antibiotics at time of surgery and 6 and 12 hours postoperatively **Surgical time** Average surgical time was 44 (range, 38 to 52) minutes in OATS group and 38 (range, 29 to 43) minutes in MF group (P < 0.07) **Co-interventions** • All patients hospitalized for 2 days after surgery and then underwent identical rehab protocol • Non-weight bearing with crutches for first 4 weeks • Partial weight bearing from 4 to 8 weeks (20 kg) • Full weight bearing after 8 weeks • Emphasized full range of motion in first few days • No postoperative brace was used • Depending on clinical exam patients allowed to return to sports 4 to 6 months postoperatively	
Gudas (2006)†							•
Gudas (2009)	RCT LoE: IIb Funding: NR	Mean F/U: 37.1 months (range 36 to 38) F/U rate 94% • 3 patients moved and were lost to F/U	N = 50 children (50 knees) Age: 24.3 OATS n = 25 60% male Average age: 14.6	Inclusion: • Grades 3 to 4 OCD lesion of the medial or lateral femoral condyle • OCD defects between 2 and 4 cm²	**Etiology:** 100% OCD **Size** (cm²) Mean: Total —, MF 3.17 ±.38, OAT 3.20 ± 34 2 cm²: Total 15/47, MF 9/22, OAT 6/25 2-3 cm²: Total 26/47, MF 12/22, OAT 14/25	Arthroscopy carried out on all patients to determine suitability for study protocol **MF** • Arthroscopic • Exposed bone debrided of all remaining unstable and necrotic bone	• International Cartilage Repair Society (ICRS) cartilage-injury grading system • Tegner activity scale • Infection

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics				Interventions and co-interventions	Outcomes
			(range, 12-18) years Tanner stage 2: 6/25 Tanner stage 3: 10/25 Tanner stage 4-5: 9/25 Microfracure n = 22 59% male Average age: 14.1 (range, 12-18) years Tanner stage 2: 9/22 Tanner stage 3: 8/22 Tanner stage 4-5: 5/22 Mean duration of symptoms: 23.54 ± 4.24 months (P = 0.2) Comorbidities: NR Classification: International Cartilage Repair Society (ICRS) cartilage-injury grading system Co-existing abnormalities: NR	• Age < 18 years • Unsuccessful 6 months of conservative treatment	3-4 cm²	6/47	1/22	5/25	• Awl used to make multiple holes or microfracures in subchondral bone plate • Holes were made as close together as possible, taking care not to break into another and thus damage • Holes approximately 2 to 4 mm wide and as close as possible to each other • Prophylactic antibiotics at time of surgery and 6 and 12 hours postoperatively **OATS** • Arthroscopic • Remnants of residual fibrotic tissue of subchondral bone were removed from the defect • Autografts harvested were 5 and 6 mm diameter plugs from lateral and/or medial margin of the femoral trochlea • Donor transplant was harvested with a larger (0.1-mm) cylinder, and lesion was carved out with a smaller cylinder, so press-fit transplantation of the osteochondral cylinder could be achieved • Average of 4.7 osteochondral plugs (range, 3 to 7 plugs) used • Prophylactic antibiotics at time of surgery and 6 and 12 hours postoperatively **Co-interventions** • Rehab identical for both techniques	
					Anatomical distribution on femoral condyle					
					MFC	41/47	20/22	21/25		
					LFC	6/47	2/22	4/25		

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
						• On second postoperative day self-assisted mobilization done until 90° of flexion attained • Controlled mobilization exercised with reduced range of motion, early isometric and isotonic exercises, and controlled mechanical compression performed • Non-weight bearing with crutches for first 2 weeks • Weight touchdown bearing from 3 to 8 weeks with most patients achieving full weight bearing by 6 weeks • At 3 to 4 months after surgery, the goal was to return to running through proprioceptive, strength, and endurance exercises and aerobic training • Return to sports allowed no sooner than 6 months after surgery	

ACI: autologous chondrocyte implantation; CMP: chondromalacia patella; DVT: deep vein thrombosis; LFC: lateral femoral condyle; LoE: level of evidence; LTC: lateral tibial condyle; MF: microfracture; MFC: medial femoral condyle; NR: not reported; OATS: osteochondral autologous transplantation system; OCD: osteochondritis dissecans;

*Only 23/44 patients had surgery (n = 11 mosaicplasty; n = 12 ACI): 14 patients had spontaneous improvement in 6-month period from debridement to scheduled surgery, 2 patients refused surgery for personal reasons, and 5 patients did not show up for presurgery exam and could not be traced

†Gudas (2006) uses the same population as Gudas (2005)

RESULTS

Table G2: Results of RCTs comparing OATS/mosaicplasty with other interventions in the knee

<table>
<tr><th>Author (year)</th><th>Repair – cartilage development</th><th>Knee specific functional outcomes</th><th>General functional outcomes</th><th>Reduced pain and other symptoms</th><th>QoL and other patient reported outcomes</th><th>Subsequent surgery</th><th>Adverse events and complications</th></tr>
<tr><td colspan="8">OATS/mosaicplasty versus autologous chondrocyte implantation (ACI)</td></tr>
<tr><td>Bentley (2003)</td><td>
International Cartilage Research Society (at second-look arthroscopy) (1 year)
<table>
<tr><td>Grade</td><td>ACI</td><td>Mosaic</td></tr>
<tr><td>1</td><td>6/37</td><td>0/23</td></tr>
<tr><td>2</td><td>24/37</td><td>8/23</td></tr>
<tr><td>3</td><td>6/37</td><td>10/23</td></tr>
<tr><td>4</td><td>1/37</td><td>5/23</td></tr>
</table>
Grades 1 or 2: 81% (30/37)* of ACI versus 34% (8/23) of moasicplasty at 1 year (P < 0.01)

Description of patients with “poor” results (ie., Cincinnati Rating System scores < 30):
Mosaicplasty: 17% (7/42) had poor results. Plugs not covered with continuous fibrous tissue (4 patients); completely disintegrated plugs (3 patients), subchondral bone exposed at margins of defect (1 patient).
Descriptive findings of second-look arthroscopy:
ACI: most patients had good filling of the defect
</td><td>
Cincinnati Rating System and Stanmore Rating System (1 year)
<table>
<tr><td></td><td>ACI</td><td>Mosaic</td></tr>
<tr><td>Excellent (> 80)</td><td>23/58</td><td>9/42</td></tr>
<tr><td>Good (55–79)</td><td>28/58</td><td>20/42</td></tr>
<tr><td>Fair (30–45)</td><td>7/58</td><td>6/42</td></tr>
<tr><td>Poor (<30)</td><td>0/58</td><td>7/42</td></tr>
</table>
Excellent or good result: 88% (51/58) ACI versus 69% (29/42) mosaicplasty at 1 year (P = 0.277)

Cincinnati Rating System and Stanmore Rating System (%) by distribution of defect
<table>
<tr><td></td><td>ACI</td><td>Mosaic</td></tr>
<tr><td>MFC</td><td></td><td></td></tr>
<tr><td>Excellent</td><td>11/24</td><td>6/29</td></tr>
<tr><td>Good</td><td>10/24</td><td>15/29</td></tr>
<tr><td>Fair</td><td>3/24</td><td>4/29</td></tr>
<tr><td>Poor</td><td>0/24</td><td>4/29</td></tr>
<tr><td>P = 0.032</td><td></td><td></td></tr>
<tr><td>LFC</td><td></td><td></td></tr>
<tr><td>Excellent</td><td>7/13</td><td>2/5</td></tr>
<tr><td>Good</td><td>5/13</td><td>0/5</td></tr>
<tr><td>Fair</td><td>1/13</td><td>2/5</td></tr>
<tr><td>Poor</td><td>0/13</td><td>1/5</td></tr>
<tr><td>P = 0.182</td><td></td><td></td></tr>
<tr><td>Patella</td><td></td><td></td></tr>
</table>
</td><td>NR</td><td>NR</td><td>NR</td><td>Group not specified:
Three patients were slow to mobilize and required manipulation under anesthesia
One patient required additional scope to mobilize the knee</td><td>See general functional outcomes column for description surgical site in those patients with poor functional outcomes.

Group not specified:
One patient developed deep vein thrombosis
One patient had superficial infection</td></tr>
</table>

Author (year)	Repair – cartilage development	Knee specific functional outcomes			General functional outcomes	Reduced pain and other symptoms	QoL and other patient reported outcomes	Subsequent surgery	Adverse events and complications
	with good incorporation, however half of the patients had soft tissue upon probing • Mosaicplasty: results varied from "very satisfactory" to "incomplete healing"	Excellent	5/20	0/5					
		Good	12/20	3/5					
		Fair	3/20	0/5					
		Poor	0/20	2/5					
		$P = 0.076$							
		Trochlea							
		Excellent	0/1	1/2					
		Good	1/1	1/2					
		Fair	0/1	0/2					
		Poor	0/1	0/2					
		Lateral tibial plateau							
		Excellent	0/0	0/1					
		Good	0/0	1/1					
		Fair	0/0	0/1					
		Poor	0/0	0/1					
Horas (2003)	Descriptive results of biopsy/second-look arthroscopy (histological results) were reported for a subset of patients, beyond scope of this HTA: ACI • Second-look arthroscopy and biopsy (5/20 or 8/20, inconsistency in report), (within 24 months postop) OATS • Second-look arthroscopy & biopsy (3/20 at 3 months, 2/20 at 21–22 months)	**Lysholm Knee Scoring Scale**			• NR	• 1/20 ACI patient, who had the largest defect treated (5.6 cm^2) complained of increased pain and was found to have partial transplant failure • 5/7 OATS patients with harvest from posterior aspect of femoral condyle had pain when squatting • When cylinder taken from anterior-superior part of medial condyle, patients only had mild pain during SLR and tenderness in the patellofemoral joint with knee extended; except for mild pain,	• Slight improvement* (24 months): ACI (2/20) vs OATS (3/20) • Substantial improvement* (24 months): ACI (17/20) vs OATS (17/20) *Definitions of slight and substantial improvement not provided	• Arthroscopy: ACI (7/20) vs OATS (8/20) • Lateral release: ACI (1/20) vs OATS (0/20) •	• 1/20 ACI patient with partial transplant failure went on to have transplant of two 9-mm osteochondral cylinders • Drainage at donor site: ACI (0/20) vs OATS (1/20) (bleeding)
			ACI	OATS					
		Pre-op	24.90	28.45					
		3 mos	27.55	27.95					
		6 mos	45.75	53.45					
		12 mos	57.50	68.25					
		24 mos	66.75	72.70					
		ACI versus OATS at 6 mos ($P \leq 0.015$), 12 mos ($P \leq 0.001$), and 24 mos ($P \leq 0.012$)							
		Tegner Activity Level Rating							
		Pre-op	1.60	1.60					
		3 mos	1.55	1.55					
		6 mos	2.95	3.55					
		12 mos	4.25	5.00					
		24 mos	5.10	5.20					
		Meyers Knee-Rating Scale							
		Pre-op	7.20	7.85					
		3 mos	8.50	7.85					
		6 mos	12.05	13.75					
		12 mos	14.15	15.90					
		24 mos	15.90	16.75					

Author (year)	Repair – cartilage development	Knee specific functional outcomes	General functional outcomes	Reduced pain and other symptoms	QoL and other patient reported outcomes	Subsequent surgery	Adverse events and complications
				symptoms disappeared by 12 weeks			
Dozin (2005)	NR	**Lysholm Knee Scoring Scale (1 year)** ACI: <60: 1/22; 60-90: 5/22; 90-100: 10/22; Subjective Improvement: 3/22; Lost to follow-up: 3/22; Total: 16/22 Mosaic: <60: 0/22; 60-90: 2/22; 90-100: 15/22; Subjective Improvement: 1/22; Lost to follow-up: 4/22; Total: 17/22 x^2 for heterogeneity = 4.92; P = 0.295; Chi sq. is for 5 groups: <60, 60-90, 90-100, subj improve, LTFU Functional status directly evaluated in 33 patients (12 ACI, 11 mosaic, 10 spontaneous improvement patients), not evaluated in 4 spontaneous improvement patients **Lysholm Knee Scoring Scale (1 year)** ACI: Failure (<60): 1/19; Partial success (60 - 90): 5/19; Complete success†: 13/19 Mosaic: Failure (<60): 0/18; Partial success (60 - 90): 2/18; Complete success†: 16/18 x^2 for heterogeneity = 2.82; P = 0.093 All categories used (failure, partial success, and total success) need to be defined †Patients who reported either Lysholm of 90-100 or subjective	NR	NR	NR	NR	NR

<table>
<tr><th>Author (year)</th><th>Repair – cartilage development</th><th>Knee specific functional outcomes</th><th>General functional outcomes</th><th>Reduced pain and other symptoms</th><th>QoL and other patient reported outcomes</th><th>Subsequent surgery</th><th>Adverse events and complications</th></tr>
<tr><td></td><td></td><td>improvement of symptoms</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="8">OATS/mosaicplasty vs. microfracture</td></tr>
<tr><td>Gudas (2005)</td><td>
International Cartilage Repair Society scores
<table>
<tr><th></th><th>MF</th><th>OATS</th></tr>
<tr><td>Preop</td><td>50.8 ± 4.07</td><td>50.7 ± 4.05</td></tr>
<tr><td>12 mos</td><td>75.6 ± 4.6</td><td>85.9 ± 4.7</td></tr>
<tr><td>24 mos</td><td>75</td><td>88</td></tr>
<tr><td>36 mos</td><td>75</td><td>89</td></tr>
</table>
MF: Preop versus 12 mos (P < .05), 24 mos (P < .05), and 36 mos (P < .05)

OATS: Preop versus 12 mos (P < .001), 24 mos (P < .001), and 36 mos (P < .001).

MF versus OATS at Preop (P = Not significant), 12 mos (P < .03), 24 mos (P < .001), and 36 mos (P < ,001).
MF patients with lesions in central part of MFC and patients with lesion > 2 cm² had worse clinical results than patients with lesions in other areas of weight-bearing parts of knee joint (P < .05)
Full thickness defects had better clinical results (according to ICRS) than did OCD (P = .004)
</td><td>
Hospital for Special Surgery score
<table>
<tr><th></th><th>MF</th><th>OATS</th></tr>
<tr><td>Preop</td><td>77.2 ± 8.12</td><td>77.9 ± 6.23</td></tr>
<tr><td>12 mos</td><td>83</td><td>88</td></tr>
<tr><td>24 mos</td><td>82</td><td>91</td></tr>
<tr><td>36 mos</td><td>80.6 ± 4.55</td><td>91.1 ± 4.15</td></tr>
</table>
MF: Preop versus 12 mos (P < .05), 24 mos (P < .05), and 36 mos (P < .05)

OATS: Preop versus 12 mos (P < .001), 24 mos (P < .001), and 36 mos (P < .001).

MF versus OATS at Preop (P = Not significant), 12 mos (P < .05), 24 mos (P < .01), and 36 mos (P < .01).
Age < 30 associated with improved functional outcomes irrespective of treatment group (P = .008) (data NR)
</td><td>96% (27/28) of OATS pts had excellent or good results compared with 52% (15/29) MF patients (P < .0001).</td><td>NR</td><td>NR</td><td>
9/29 failures in MF group requiring revision surgery; 8 had loosening fibrocartilage tissue from defect requiring OATS procedure and 1 had arthrofibrosis requiring debridement (patients symptomatic)
1/28 failure in the OATS group required substitution of one osteochondral plug (patient symptomatic)
Second-look arthroscopies due to further injuries performed in 5 OATS pts and 3 MF pts that then required further surgical intervention
</td><td>
2/28 cases of superficial infection in OATS group
No donor-site morbidity in OATS group
No graft loosening/migration in OATS group (radiography, 12 months)
No arthritic changes in any patients (radiography, 12 months)
Subchondral cysts
</td></tr>
</table>

<table>
<tr><th>Author (year)</th><th>Repair – cartilage development</th><th>Knee specific functional outcomes</th><th>General functional outcomes</th><th>Reduced pain and other symptoms</th><th>QoL and other patient reported outcomes</th><th>Subsequent surgery</th><th>Adverse events and complications</th></tr>
<tr><td></td><td>• Age < 30 associated with improved clinical outcomes irrespective of treatment group (P = .008) (data NR)
• Second-look arthroscopies performed at mean of 12.4 (range, 10, 21) months: 9 vs 1 failure (MF (n = 20) vs OATS (n = 14))
• Biopsies performed in 25 patients (OATS (14/28), MF (14/29))
• Thickness of repair tissue (radiography at 12 months):
• Joint surface congruency (radiography at 12 months):
• Regularity of donor site surface in OATS patients (radiography at 12 months):</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Gudas (2009)</td><td>International Cartilage Repair Society score<table><tr><td></td><td>MF</td><td>OATS</td></tr><tr><td>Preop</td><td>51</td><td>51</td></tr><tr><td>12 mos</td><td>86</td><td>92</td></tr><tr><td>24 mos</td><td>75</td><td>84</td></tr><tr><td>36 mos</td><td>64</td><td>84</td></tr><tr><td>48 mos</td><td>63</td><td>83</td></tr></table>MF: Preop versus 12 mos (P < .05), 24 mos (P < .05), and 36 mos (P < .05)

OATS: Preop versus 12 mos (P < .001), 24 mos (P < .001), and 36 mos (P < .001).

MF versus OATS at Preop (P = Not significant), 36 mos (P < .001).</td><td>• 7/22 MF patients achieved preinjury activity level at 14.1 months, but only 3 of the patients remained at the same level after 4.2 years
• 21/25 of OATS patients achieved preinjury activity level at 11.7 months , and 81% were practicing sports at the same level after 4..2 years</td><td>NR</td><td>NR</td><td>NR</td><td>• 9/22 failures in MF group requiring revision surgery; 7 underwent OATS procedure and 2 had treated with the autologous chondrocyte implantation procedure
• 0/25 failures in the OATS group</td><td>• 1/25 case of superficial infection in OATS group</td></tr>
</table>

Author (year)	Repair – cartilage development	Knee specific functional outcomes	General functional outcomes	Reduced pain and other symptoms	QoL and other patient reported outcomes	Subsequent surgery	Adverse events and complications
	MF group showed significant deterioration over 4.2 year follow up ($P < .05$) • Patients in the MF group with a lesion larger than 2 cm² had significantly worse clinical results that those with a lesion smaller than 3 cm² ($P < .05$) • This association was not found in the OATS patients ($P > .05$) • MRI evaluation according to the ICRS evaluation system showed excellent or good repairs in 19/ 21 (91%) OATS compared with 10 of 18 (56%) after MF						

ICRS: International Cartilage Research Society; SLR: straight leg raise

*Bentley 2003: there was a discrepancy between the results presented in the table (31/37) and the text (30/37) regarding the number of patients in the ACI group who had ICRS grades of 1 or 2. Here we reported data from the table, as the number of patients with each ICRS grade added up to the appropriate total number of patients in the ACI group.

‡Gudas (2006) uses the same population as Gudas (2005)

Appendix H. Non-Randomized Comparative Studies – Data Abstraction

The first set of tables describes demographics and study design. The second set of tables describes the results

DEMOGRAPHICS AND STUDY DESIGN

Table H1: Characteristics of non-randomized comparative studies of OATS/mosaicplasty with other interventions in the knee

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
Knee – Osteochondral defect							
Gaweda & Mazurkiewicz (2006)	Prosepective Funding: NR	F/U: NR	N = 49 Chondral defects graded by ICRS as Grade I or II and receiving only patellar realignment (control) n = 30 Mean age: 21.7 years Chondral defects graded by ICRS as Grade III or IV receiving patellar realignment and osteochondral grafting (study) n = 19 Mean age: 25.5 years Mean number of dislocations: • Control: 6/30 • Study: 11/19	Inclusion: Patients scheduled for extensor realignment between February 2001 and February 2003. Exclusion: All patients were treated surgically by realignment but without severe patellar chondral defectsas controls. In the control group, there were no patients with chondral lesions above grade I or II according to the ICRS.	Chondral defects as graded by the International Cartilage Repair Society • Defects Grade I or II (n = 30) • Defects Grade III or IV (n = 19)	• A lateral parapatellar approach was used. The proximal part of the realignment consisted of lateral release and reattachment of the vastus medialis muscle. The medial retinaculum was reefed • Transfer of the tibial tubercle was performed in the distal part • The tubercle was osteotomized only proximally; displaced medially by force leaving its thin, distal cortical attachment intact as the hinge • Fixed in the newly prepared position with two cancellous screws • Joint surfaces were examined • For osteochondral grafting, SDS and Mosaicplasty grafting tools were used • Mean number of grafts was 3 • The grafts were harvested from the lateral margin of the lateral femoral condyle Co-Intervention • Postoperative regime did not differ between groups • For the first 1-2 weeks, patients were immobilized using a long-leg cast or orthosis	• Marshall Score • Range of motion

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
						• Walking was allowed after 2-3 days using crutches and partial weight bearing • Patients instructed about quadriceps wisometric and straight-leg-raising exercises • Passive and active range of motion exercises were started after five weeks	
Gaweda & Patyra (2006)	Cohort LoE: Funding: NR	Study group: Mean F/U: 17.1 months (range, 12-34 months) Control group: Mean F/U: 19.1 months (range, 12-36 months) % F/U: NR	Study group*: N = 21 Sex: 19 men (90%), 2 women Age: 30.87 years *Combined ACL reconstruction and osteo-chondral grafting in 1 step Control group**: N = 32 Sex: 22 men (69%), 10 women Age: 33.12 years **Isolated ACL reconstruction	Inclusion: Study Group: -Chronic ACL deficiency -Grade III or IV cartilage lesions according to the ICRS scale Control Group: -Chronic ACL insufficiency -No chondral deficit higher than grade I on the ICRS scale	Study group: **Lesions:** MFC: 19 LFC: 1 Both condyles: 1 **Average size of defects:** 1.52 cm^2 2.45 osteochondral plugs (range, 1-6) - Diameter of plugs: range, 4.5 – 8.5 mm Control group: -ACL reconstruction	• All procedures were performed via arthrotomy by the same team of surgeons • Interference screws were used for the LP grafts (12 in study group, 9 in control group) • An endo-button proximally and a cancellous screw distally were used for the ST+GR grafts (9 in study group, 23 in control group) • Rehabilitation: both groups used a long brace (0-30° ROM) post-op, then, as tolerated, 2 crutch ambulation (non-weight-bearing first 7-14 days, then full-weight-bearing after 4-6 weeks). • Rehab protocol was modification of Hangody and Fules, and Shelbourne and Gray	• Lysholm and Gillquist score • Marshall score
Pascual-Garrido (2009) ALLOGRAFT	Prospective Cohort LoE: Funding: NR	Mean F/U: 4 years (± 1.8 years; range 2-10) F/U rate 88.5% 46/52 (6 lost to F/U)	N = 46 patients (48 cases of OCD) Average patient age: 34 years (range; 20-49)	Inclusion: Diagnosed and surgically treated OCD of the knee Exclusion: < 20 years old at time of surgery	Mean defect size: • 4.5 ± 2.7 cm^2 (range, 0.9-15 cm^2) Lesion distribution: • MFC: 37/48 • LFC: 8/48 • Both condyles: 3/48	• The spectrum of surgical procedures included 1 debridement, consisting of shaving for mechanical removal of loose flaps and debris until stable borders were obtained; 9 fragment excision (loose-body removal) for those cases in which the fragment could not be initially stabilized; 2 in situ drilling; 15 ARIF; 2 microfracture; 16 fresh osteochondral allograft (graft size: 18-25 mm diameter and 6-8 mm depth); and 3 ACI.	• Noyes • Tegner • Lysholm • International Knee Documentation Committee • Knee Injury and Osteoarthritis Score o Pain o Other Disease-specific symptoms o ADL o Sport and recreation function

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
							o Knee-related QoL • Short-Form-12
Salzmann (2009)	Prospective Cohort LoE: Funding: NR	F/U: 100% (18/18) F/U length: 41.6 (range, 23-77) months	Total: N = 18 Male: 16 (89%) Mean age: 33.8 years Matrix-assisted chondrocyte transplantation (MACT) group: N = 9 Male: 8 (89%) Mean age: 32.7 ± 7.2 years • Post-op interval: 42.0 ± 17.4 (range, 25-77) months • ICRS 3-4a lesions • Defect size about 3cm^2 • 7 previous traumatic events • 2 reported subtle symptom imrovement Autologous osterochondral autograft transplantation (OCT) group: N = 9 Male: 8 (89%) Mean age: 33.9 ± 7.5 years • Post-op interval: 41.3 ± 16.5 (range, 23-75) months • ICRS 4a, 4b lesions • Defect size less than 3cm^2 • 3 previous osteochondritis dissecans • 1 previous patellar flake	Inclusion: • Patients who underwent MACT or OCT for treatment of cartilage defects at the knee joint Exclusion • Obesity (BMI > 35) • OA (>grade 1 according to the Kellgren and Lawrence classification) • Rheumatoid arthritis • Absence or extensive mensical loss • Ligamentous instability • Active local or systematic infections • Inflammatory arthropathy • Varus or valgus deformity of more than 2˚ • Limited ROM with active knee flexion below 120˚ or an extension deficiency exceeding 15˚	Cartilage defect localization: • Medial femoral condyle: o 6 MACT o 6 OCT • Patella: o 2 MACT o 2 OCT • Lateral femoral condyle: o 1 MACT o 1 OCT MACT patients: • 4 ICRS 3 lesions o 3 medial femoral condyle o 1 patella • 5 ICRS 4a lesions o 3 medial femoral condyle o 1 patella o 1 lateral femoral condyle OCT patients: • 6 ICRS 4a lesions o 5 medial femoral condyle o 1 patella • 3 ICRS 4b lesions o 1 medial femoral condyle o 1 lateral femoral condyle o 1 patella Mean defect size: • OCT: 2.3 (0.9-2.6) cm^2 • MACT: 6.3 (3-12) cm^2	• All MACT patients were arthroscopically assessed and the cartilage biopsy for chondrocyte isolation and expansion was harvested within the first procedure • The second stage of MACT transplantation was performed by use of an open approach • The cartilage defects in all OCT patients were assessed arthroscopically and subsequently treated by an open approach	• Modified Lysholm score • Modified Cincinnati knee rating system • Visual analog scale (VAS) for pain • Tegner activity scale • Short-Form 36 (SF-36)

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
			fracture • 2 traumatic events • 3 subtle symptom improvement • Diameter of transplanted cylinders = 10 mm in every patient • Mean number of 1.5 ± 1.0 transplanted cylinders				
Rue (2008)	Case-series LoE: IV Funding: NR Conflict of interest:	Mean F/U: 3.1 years (range,) F/U rate 94% (29/31) • 2 patients were lost to follow-up.	N = 31 (31 knees) Mean age: 29.9 years (range, 13.9 – 49.9 years) 58% male Meniscal allograft transplantation (MAT) combined with autologous	Inclusion: • Persistent symptoms after menisectomy with combined articular cartilage injury, • Normal alignment or correction to normal alignment,	**Etiology: 100%** combined articular cartilage injury. Mean chondral lesion size (cm^2) Total (range) 4.68 (1.80 - 9.50) ACI (range) 3.93 (1.80 - 7.50) OAT (range) 5.48 (2.24 - 9.50)	• All patients were recruited from a pool of patients having had menisectomy. • All menisci in the medial compartment were transplanted using a double bone plug technique as described by Shelton and Dukes.	• Lysholm • Tenger • Noyes - Sports activity - Symptom • IKDC (international Knee Documentation Committee) • KOOS, Knee Injury

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
	coauthor Cole is a consultant for Genzyme (ACI manufacturer)		chondryte implantation (ACI) (ACI group) n = 16 % male Average age: (range,) years MAT with oesteochondral allograft implantation (OAT) (OAT group) n = % male Average age: (range,) years Mean duration of symptoms: 23.54 ± 4.24 months (P = 0.2) Comorbidities: NR Classification: International Cartilage Repair Society (ICRS) cartilage-injury grading system Co-existing abnormalities: NR	• Stable ligamentous knee examination.		• All menisci in the lateral compartment were transplanted using the keyhole technique as described by Goble et al. • All Mat were performed using a bridge-in-slot technique. • The majority of menisci were cryopreserved • Those placed after 2004 were fresh-frozen. • Autologous chrondocyte transplantation was performed as described by jones and Peterson. • OAT was performed according to established protocols. The decision to proceed with ACI or OAT was made by the senior surgeon based on patient age and the location size, and depth of the lesion: **ACI** • ACI was chosen for relatively younger patients with superficial defects especially of the pattelofemoral join. **OATS** Fresh OA grafts were chosen for older patients with larger defect of the femoral condyle with associated bone loss. • **Co-interventions** All patients in this study had the same rehab. • Posteroperatively, all patients were	and Osteoarthirtis Outcome Score o Pain o Symptom o ADL, activities of daily living o Sports o QOL, quality of life • SF short form o Physical o Mental

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
						placed in a hinged knee braced locked in full extension. • 6 weeks of nonweightbearing exercises, with the use of a continuous passive motion machine in 3-hour increments for 6 to 8 hours per day. • The brace was gradually opened at 4 to 6 weeks to allow progression flexion as quadriceps control returned	

Table H2. Characteristics of non-RCTs comparing OATS/mosaicplasty with other interventions in the ankle/talus

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
Mosiacplasty versus autologous chondrocyte implantation (ACI)							
Gobbi (2006)	Cohort LoE: I or II* Funding: NR	<u>Chondroplasty treatment group</u> Mean F/U: <u>Microfracture treatment group</u> Mean F/U: <u>OAT treatment group</u> Mean F/U:	N = 32 patients <u>Chondroplasty</u> n = 11 56% male Mean age: 32 years (range, 19-45 years) <u>Microfracture</u> n = 9 67% male Mean age: 24 years (range, 17-28 years) <u>OAT</u> n = 12 66% male Mean age: 27.8 years (range, 21-53 years)	Inclusion: • Patients with Ferkel class 2b, 3 and 4 OLT with symptoms of ankle pain or limitation of function despite a minimum of 6 months of nonsurgical management. • Only primary cases with no previous surgical treatment for OLT were included. Exclusion: • Patients with lesions smaller than 1cm^2 in diameter • Bipolar (kissing) lesions • Diffuse arthiric changes • Associated ankle disease (e.g., ankle fracture) • Far posterior or central lesions not realidy amendable to arthroscopic management	**Size (cm^2)** **Chrondroplasty (range)**: 4 (1-6) **Microfracture (range)**: 4.5 (1.5-8) **OAT (range)**: 3.7 (1.2-5) **Location – Lateral (n/n total)** 7/11 | 7/10 | 8/12 **Location – Medial (n/n total)** 4/11 | 3/10 | 4/12 **Lesion Ferkel class – IIb (n/n total)** 3/11 | 2/10 | 0/12 **Lesion Ferkel class -- III (n/n total)** 4/11 | 3/10 | 4/12 **Lesion Ferkel class -- IV (n/n total)** 4/11 | 5/10 | 8/12 **ACT (range)**: 20 x 16.2 (35-15 x 25-15) **AOT (range)**: 16.5 x 15 (25 x 10 x 20-10) **Depth (mm)**	Intervention procedure: <u>Chondroplasty:</u> • Arthroscopy • Loose chondral or oesteochondral framents excised • Mechanical shaver used to trim damaged cartilage with goal of creating a smooth articular suragece <u>Microfracture:</u> • Performed with Microfracture awl • Unstable condral fragment excised with arthroscopic shaver or handheld curette • Subchondral bone was debrided of the calcific layer • Multiple perforations perpendicular to the join surgace were placed 3 to 4mm apart to a dept that allowed observation of fat droplets and blood from the perforations when arthroscopic irrigation fuid pump pressure was lowered <u>OAT:</u> • Performed with mosaicplasty autogenous oesteochondral grafting system • Unstable chondral	• AOFAS Ankle Hindfoot Scale (primary outcome measure, range 0 to 100, with a score of 100 indicating full mobility, good alignment and no pain) postoperatively at 12 and 24 months. • Single Assessment Numeric Evaluation (range, 0 to 100) performed postoperatively and at final follow-up • MRI evaluation 12 months postoperatively

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes
					7 | 4	fragments were removed with an arthroscopic shaver of handheld curette • Measurement of the lesions with sizers of variable diameters • Total of 1 to 3 osteochondral plugs were then harvested (from the periphery of the lateral femoral condyle or the trochlear notch of the ipsilateral knee) and were transplanted to the lesion in a particular position, such that articular surfaces were level with the adjacent talar dome. Co-interventions: • Post-operatively, all ankles immobilized in a brace for 7 days • Followed by unrestricted, active range of ankle motion • Non-weight bearing for 8 weeks • No sports or impact activity for 6 months	

RESULTS

Table H3: Results of non-RCTs comparing OATS/mosaicplasty with other interventions in the knee

Author (year)	Repair – cartilage development	Knee specific functional outcomes	General functional outcomes	Reduced pain and other symptoms	QoL and other patient reported outcomes	Subsequent surgery	Adverse events and complications
Knee – Osteochondral defect							
Gaweda & Mazurkiewicz (2006)	NR	**Mean Marshall Score** Preop: Control 40.7 ± 3.7; Study 36.3 ± 2.1 6 week: Control 30.1 ± 2.5; Study 28.6 ± 2.4 3 mos: Control 35.8 ± 3.4; Study 32.7 ± 1.8 6 mos: Control 41.6 ± 3.8; Study 39.7 ± 1.8 12 mos: Control 45.7 ± 2.5; Study 45.1 ± 1.5 24 mos: Control 47.1 ± 1.6; Study 46.2 ± 1.8	**Range of motion** Preop: Control 40.7 ± 3.7; Study 36.3 ± 2.1 6 week: Control 30.1 ± 2.5; Study 28.6 ± 2.4 3 mos: Control 35.8 ± 3.4; Study 32.7 ± 1.8 6 mos: Control 41.6 ± 3.8; Study 39.7 ± 1.8 12 mos: Control 45.7 ± 2.5; Study 45.1 ± 1.5 24 mos: Control 47.1 ± 1.6; Study 46.2 ± 1.8	NR	NR	Study Group: • Manipulation under general anesthesia for one patient, four months after surgery. • 1 patient had repeat arthroscopy due to loosening of an osteochondral pin from the patellae 2 months postoperatively. Control Group: • Two manipulations were performed 6 and 8 months postoperatively.	Patients in the study group suffered more often from crepitus and 'clicks' during knee movement and had a tendency for joint effusion more frequently than the control group.
Gaweda & Patyra (2006)	Assessed: -preop -6 weeks -3 months -6 months -12 months	L&G Score: Mean (at 12 month): Study 89.19 ± 3.65 points (p<0.001); Control 93.84 ± 2.87 points (p<0.001) 12mo - initial (mean gain): Study 30.66 ±7.79; Control 31.65 ± 6.96 Marshall Score: Mean (at 12 month): Study 43.24 ± 1.79 (p<0.001); Control 44.81 ± 2.4 (p<0.001) 12mo - initial (mean gain)*: Study 9.05 ± 3.81; Control 10.71 ± 3.43 *significant difference (p=0.49)	NR	NR	**NR**	-1 case of infection around the distal fixation screw which had to be removed after 3 months in control group	Study group: -3 complained of minor prolonged pain 12 months post-op -Joint oedema and effusions were common up to 6 months post-op -5 had recurrent joint effusions related to extensive activity up to 18 months post-op Control group: -1 manipulation under anesthetic was required 6 months after operation to increase flexion beyond 90° -2 patients had steroid injections (1 and 3 injections) for persistent irritation of the mucosa

<table>
<tr><th>Author (year)</th><th>Repair – cartilage development</th><th>Knee specific functional outcomes</th><th>General functional outcomes</th><th>Reduced pain and other symptoms</th><th>QoL and other patient reported outcomes</th><th>Subsequent surgery</th><th>Adverse events and complications</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>and joint effusion
-1 case of post-op joint infection
-1 case of infection around the distal fixation screw which had to be removed after 3 months
-1 ruptured the reconstructed ligament 18 months post-op (then lost to F/U)
-1 developed deep vein thrombosis of the operated leg 3 months post-op</td></tr>
<tr><td>Pascual-Garrido (2009)
ALLOGRAFT</td><td></td><td>Pre and postop scores for patients with OCD OF LFC
<table><tr><th></th><th>Pre</th><th>Post</th><th>P</th></tr><tr><td>Tegner</td><td>1</td><td>4</td><td>.020</td></tr><tr><td>LKS</td><td>28</td><td>36</td><td>.040</td></tr><tr><td>IKDC</td><td>31</td><td>55</td><td>.034</td></tr><tr><td>KOOS</td><td></td><td></td><td></td></tr><tr><td>Pain</td><td>57</td><td>86</td><td>.012</td></tr><tr><td>Symp</td><td>50</td><td>80</td><td>.007</td></tr><tr><td>ADL</td><td>54</td><td>85</td><td>.034</td></tr><tr><td>Sport</td><td>31</td><td>68</td><td>.034</td></tr><tr><td>QOL</td><td>24</td><td>57</td><td>.023</td></tr><tr><td>SF-12</td><td></td><td></td><td></td></tr><tr><td>Mental</td><td>40</td><td>43</td><td>.370</td></tr><tr><td>Phys</td><td>42</td><td>52</td><td>.112</td></tr></table>Outcomes of ARIF vs LBR vs OA graft
Tegner
<table><tr><th></th><th>Pre</th><th>Post</th><th>P</th></tr><tr><td>ARIF</td><td>2</td><td>3</td><td>.430</td></tr><tr><td>LBR</td><td>1</td><td>5</td><td>.032</td></tr><tr><td>OA</td><td>0</td><td>6</td><td>.001</td></tr></table>p-value = .034; ARIF < OA graft
LKS
<table><tr><th></th><th>Pre</th><th>Post</th><th>P</th></tr><tr><td>ARIF</td><td>28</td><td>42</td><td>.008</td></tr><tr><td>LBR</td><td>32</td><td>44</td><td>.110</td></tr><tr><td>OA</td><td>25</td><td>37</td><td>.015</td></tr></table>p-value = .950</td><td>Outcomes of ARIF vs LBR vs OA graft
SF-12 Mental
<table><tr><th></th><th>Pre</th><th>Post</th><th>P</th></tr><tr><td>ARIF</td><td>53</td><td>56</td><td>.134</td></tr><tr><td>LBR</td><td>54</td><td>54</td><td>.940</td></tr><tr><td>OA</td><td>49</td><td>57</td><td>.407</td></tr></table>p-value = .260
SF-12 Physical
<table><tr><th></th><th>Pre</th><th>Post</th><th>P</th></tr><tr><td>ARIF</td><td>36</td><td>41</td><td>.002</td></tr><tr><td>LBR</td><td>36</td><td>43</td><td>.018</td></tr><tr><td>OA</td><td>41</td><td>43</td><td>.087</td></tr></table>p-value = .330</td><td>NR</td><td>NR</td><td>7 knees had clinical failure of the initial treatment and underwent revision
1 patient failed results loose-body removal and later required a microfracture.
3 patients initially treated with ARIF had failed results and were subsequently treated.
1 patient with a failed osteochondral allograft converted to a total knee arthroplasty.
1 patient failed initial drilling and needed a microfracture.
1 patient failed ACI and converted to an osteochondral allograft.
All 15 patients treated with ARIF had subsequent arthroscopy 2 months after treatment.</td><td>NR</td></tr>
</table>

<table>
<tr><th>Author (year)</th><th>Repair – cartilage development</th><th>Knee specific functional outcomes</th><th>General functional outcomes</th><th>Reduced pain and other symptoms</th><th>QoL and other patient reported outcomes</th><th>Subsequent surgery</th><th>Adverse events and complications</th></tr>
<tr><td></td><td></td><td>
IKDC
<table>
<tr><td></td><td>Pre</td><td>Post</td><td>P</td></tr>
<tr><td>ARIF</td><td>37</td><td>53</td><td>.005</td></tr>
<tr><td>LBR</td><td>37</td><td>58</td><td>.002</td></tr>
<tr><td>OA</td><td>31</td><td>45</td><td>.004</td></tr>
<tr><td colspan="4">p-value = .630</td></tr>
<tr><td colspan="4">KOOS Pain</td></tr>
<tr><td></td><td>Pre</td><td>Post</td><td>P</td></tr>
<tr><td>ARIF</td><td>65</td><td>81</td><td>.007</td></tr>
<tr><td>LBR</td><td>65</td><td>78</td><td>.092</td></tr>
<tr><td>OA</td><td>52</td><td>74</td><td>.004</td></tr>
<tr><td colspan="4">p-value = .590</td></tr>
<tr><td colspan="4">KOOS Symptoms</td></tr>
<tr><td></td><td>Pre</td><td>Post</td><td>P</td></tr>
<tr><td>ARIF</td><td>54</td><td>80</td><td>.001</td></tr>
<tr><td>LBR</td><td>55</td><td>71</td><td>.180</td></tr>
<tr><td>OA</td><td>59</td><td>67</td><td>.270</td></tr>
<tr><td colspan="4">p-value = .290</td></tr>
<tr><td colspan="4">KOOS ADL</td></tr>
<tr><td></td><td>Pre</td><td>Post</td><td>P</td></tr>
<tr><td>ARIF</td><td>72</td><td>86</td><td>.015</td></tr>
<tr><td>LBR</td><td>70</td><td>87</td><td>.025</td></tr>
<tr><td>OA</td><td>57</td><td>67</td><td>.200</td></tr>
<tr><td colspan="4">p-value = .830</td></tr>
<tr><td colspan="4">KOOS Sport</td></tr>
<tr><td></td><td>Pre</td><td>Post</td><td>P</td></tr>
<tr><td>ARIF</td><td>29</td><td>80</td><td>.001</td></tr>
<tr><td>LBR</td><td>30</td><td>77</td><td>.002</td></tr>
<tr><td>OA</td><td>32</td><td>46</td><td>.037</td></tr>
<tr><td colspan="4">p-value = .008; ARIF > OA graft and LBR > OA graft</td></tr>
<tr><td colspan="4">KOOS QoL</td></tr>
<tr><td></td><td>Pre</td><td>Post</td><td>P</td></tr>
<tr><td>ARIF</td><td>25</td><td>53</td><td>.134</td></tr>
<tr><td>LBR</td><td>26</td><td>65</td><td>.940</td></tr>
<tr><td>OA</td><td>29</td><td>39</td><td>.062</td></tr>
<tr><td colspan="4">p-value = .030; LBR > OA graft</td></tr>
</table>
</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Salzmann (2009)</td><td>NR</td><td>
<table>
<tr><td></td><td>Lysholm</td><td>Cincinnati</td><td>Tegner</td></tr>
<tr><td>MACT</td><td>77.0 ±9.9</td><td>74.3 ±16.2</td><td>5.4 ±1.9</td></tr>
<tr><td>OCT</td><td>66.8</td><td>68.3</td><td>5.0</td></tr>
</table>
</td><td>
<table>
<tr><td></td><td>SF-36 PCS</td><td>SF-36 MCS</td></tr>
<tr><td>MACT</td><td>52.4 ±2.7</td><td>52.5 ±3.4</td></tr>
<tr><td>OCT</td><td>48.8</td><td>46.6</td></tr>
</table>
</td><td>
<table>
<tr><td></td><td>VAS</td></tr>
<tr><td>MACT</td><td>1.9 ±0.8</td></tr>
<tr><td>OCT</td><td>2.5 ±2.2</td></tr>
</table>
</td><td></td><td>• NR</td><td>• NR</td></tr>
</table>

Author (year)	Repair – cartilage development	Knee specific functional outcomes	General functional outcomes	Reduced pain and other symptoms	QoL and other patient reported outcomes	Subsequent surgery	Adverse events and complications
		±9.9 ±18.3 ±2.1 95% CI -22.0 to 0.59 -21.5 to 3.6 -2.6 to 1.8 P value 0.04 0.12 0.69	±8.2 ±8.8 95% CI -12.7 to 6.0 -16.6 to 4.6 P value 0.45 0.24	95% CI -1.3 to 2.5 P value 0.49			
Rue (2008)	NR	**Lysholm Knee Scoring Scale** ACI OAT Preop 55 ± 16 42 ± 14.5 Follow-up 79.4 ± 11.9 68.2 ± 21.3 *P* (Preop versus follow-up) <.001 0.001 Follow-up comparison *P* = 0.104 in favor of ACI. Tegner Activity Level Preop 5.5 ± 2.9 4.4 ± 3.7 Follow-up 7.3 ± 1.5 6.2 ± 2.9 *P* (Preop versus follow-up) 0.026 0.03 Follow-up comparison *P* = 0.217 in favor of ACI. Noyes Sports Activity Preop 61.8 ± 26 47.3 ± 39 Follow-up 81.1 ± 10.6 67.7 ± 27.7 *P* (Preop versus follow-up) 0.018 0.036	**SF-12 – Physical** ACI OAT Preop 40.6 ± 6.3 37 ± 8.2 Follow-up 45.6 ± 3.5 42.2 ± 6.9 *P* (Preop versus follow-up) 0.009 0.081 Follow-up comparison P = 0.12 in favor of ACI. SF-12 – Mental Preop 58.2 ± 6.4 52.6 ± 11.3 Follow-up 54.7 ± 6.5 55.7 ± 9.9 *P* (Preop versus follow-up) 0.159 0.135 Follow-up comparison P = 0.773 in favor of OAT.	**KOOS – Pain** ACI OAT Preop 62.9 ± 11.9 47.3 ± 15.5 Follow-up 88.9 ± 9.4 73.1 ± 19.3 *P* (Preop versus follow-up) <.001 <.001 Follow-up comparison *P* = 0.011 in favor of ACI.	**KOOS – ADL** ACI OAT Preop 82.6 ± 8.3 60.9 ± 23.3 Follow-up 97.4 ± 2.5 84.3 ± 13.7 *P* (Preop versus follow-up) <.001 0.003 Follow-up comparison P = 0.002 in favor of ACI. Knee Injury and Osteoarthritis Outcome Score -- Symptom Preop 29.6 ± 16.8 60.9 ± 23.3 Follow-up 70.4 ± 20.5 84.3 ± 13.7 *P* (Preop versus follow-up) <.001 0.003 Follow-up comparison *P* = 0.025 in favor of ACI. Knee Injury and Osteoarthritis Outcome Score -- Sport Preop 29.6 ± 16.8 60.9 ± 23.3 Follow-up 70.4 ± 20.5 84.3 ± 13.7 *P* (Preop versus follow- <.001 0.003	• Five patients had subsequent procedures on the same knee. • Four underwent limited debridement • 3 had mild hyper trophy of their ACI patches (2 with complete fill and normal appearance, 1 with mild softening) • And 1 had mild trochlear chondral changes unrelated to his OA graft that was 100% intact. • In all 4 of these patients the MAT was documented to entirely intact with complete incorporation. • The final patients had a granuloma removed from the ipsilateral knee 18 months after her ACI/MAT.	• 3 cases of mild hypertrophy on ACI patches. • 1 case of granuloma. • No infections, neurovascular complications, or other complications associated with the procedures.

Author (year)	Repair – cartilage development	Knee specific functional outcomes	General functional outcomes	Reduced pain and other symptoms	QoL and other patient reported outcomes	Subsequent surgery	Adverse events and complications
					up)		
		Follow-up comparison *P* = 0.105 in favor of ACI.			Follow-up comparison *P* = 0.001 in favor of ACI.		
		Noyes Symptoms			Knee Injury and Osteoarthritis Outcome Score – Quality of Life (QOL)		
		Preop: 6.2 ± 1.4 / 4.5 ± 1.8			Preop: 35.7 ± 13.5 / 20.8 ± 14.8		
		Follow-up: 8.6 ± 1.2 / 7.1 ± 1.8			Follow-up: 67.9 ± 15.7 / 42.7 ± 18.8		
		P (Preop versus follow-up): <.001 / <.001			*P* (Preop versus follow-up): <.001 / 0.001		
		Follow-up comparison *P* = 0.013 in favor of ACI.			Follow-up comparison *P* = <.001 in favor of ACI.		
		International Knee Documentation Committee					
		Preop: 45.5 ± 8.2 / 31.4 ± 12.8					
		Follow-up: 76 ± 10.8 / 57.1 ± 17.8					
		P (Preop versus follow-up): <.001 / <.001					
		Follow-up comparison *P* = 0.002 in favor of ACI.					

ADL: Activites of Daily Living; IKDC: International Knee Documentation Committee; KOOS: Knee Injury and Osteoarthritis Outcome Score; QOL: Quality of Life

Table H4: Results of RCTs comparing OATS/mosaicplasty with other interventions in the knee

Author (year)	Repair – cartilage development	Knee specific functional outcomes	General functional outcomes	Reduced pain and other symptoms	QoL and other patient reported outcomes	Subsequent surgery	Adverse events and complications
OATS/mosaicplasty versus autologous chondrocyte implantation (ACI)							
Gobbi (2006)	**NR**	**NR**	SANE score Preop CP / OAT / MF	**Numeric Pain Intensity Scores** **Mean score**	Mean AOFAS score Treatment	• Revision arthroscopy was performed on one patient from the	• No other complications of significant value other than pain were

<table>
<tr><th>Author (year)</th><th>Repair – cartilage development</th><th>Knee specific functional outcomes</th><th>General functional outcomes</th><th>Reduced pain and other symptoms</th><th>QoL and other patient reported outcomes</th><th>Subsequent surgery</th><th>Adverse events and complications</th></tr>
<tr><td></td><td></td><td></td><td>38 | 35 | 36
24 month F/U
78 | 82 | 80</td><td>CP | OAT | MF
3.3 | 5.25 | 3.4</td><td>CP | OAT | MF
Preop
36.8 | 31.1 | 22.8
12 months
78.2 | 81.4 | 82.2
24 months
82.7 | 82.2 | 83.8</td><td>Chondroplasty group.
• In the OAT group, 2 patients had arthroscopic debridement for anterior fibrous impingement.</td><td>observed.
• In the CP group, 1 patient has persistent ankle pain 9 months postoperatively.
• In the OAT group, 2 patients had pain and stiffness at 8 months and 22 months postoperatively, respectively.
• No harvest site complications were observed in the OAT group.</td></tr>
</table>

	ACT	AOT
Preop	3.5 (very bad)	3.6 (very bad)
Post-op	1.1 (excellent)	1 (excellent)

CP: Chondroplasty; OAT: Osteochondral Autologous Transplantation; MF: Microfracture

Appendix I. Summary of Safety Data

Table I 1a. Complications in RCTs of osteochondral autograft transplantation

Author (year)	N	Pain	Arthrofibrosis or joint stiffness	Donor site morbidity	Hemarthrosis	Infection	Joint swelling/effusion	Subchondral cyst on MRI
Bentley (2003)*	MOS: 42 ACI: 58							
Dozin (2005)†	MOS: 22 ACI: 22							
Gudas (2005)	OAT: 28 MF: 29		OAT: 0/28 MF: 1/29 (3%)	OAT: 0/28 MF: N/A		OAT: 2/28 (7%) MF: 0/29		OAT: 2/25 (8%) MF: 7/21 (33%)
Gudas (2009)	OAT: 25 MF: 22	OAT: 9/25 (36%) MF: 13/22 (59%)				OAT: 1/25 (4%) MF: 0/25	OAT: 2/25 (8%) MF: 10/22 (45%)	
Horas (2003)	OAT: 20 ACI: 20	OAT: 3/20 (15%) ACI: 2/20 (10%)	OAT: 6/20 (20%) ACI: 3/20 (10%)	OAT: 5/20 (25%) ACI: 0/20	OAT: 2/20 (10%) ACI: 0/20	OAT: 1/20 (5%) ACI: 0/20	OAT: 1/20 (5%) ACI: 3/20 (15%)	

MOS: mosaicplasty; OAT: osteochondral autologous transplantation; ACI: autologous chondrocyte implantation; MF: microfracture

* In this study, complications were not reported separately by treatment group; among all 42 patients there was one calf-vein thrombosis, one superficial infection, 3 with joint stiffness treated with manipulation under anesthesia (one of these required arthroscopy with loosening of adhesions to mobilize)

† Did not report on complications or adverse events

Table I 1b. Revisions and re-operations in RCTs of osteochondral autograft transplantation

Author (year)	N	Arthroscopy	Revision of same procedure (e.g., replacement of plug)	Alternative cartilage repair procedure	Debridement (arthroscopic)	Release adhesions (arthroscopic)	Spongialization (arthroscopic)
Bentley (2003)*	MOS: 42 ACI: 58						
Dozin (2005)†	MOS: 22 ACI: 22						
Gudas (2005)	OAT: 28 MF: 29	OAT: 8/28 (28.6%)‡ MF: 8/29 (27.6%)‡	OAT: 1/28 (3.6%) MF: N/A	OAT: 0/28 MF: 8/29 (27.6%) (OAT)	OAT: 0/28 MF: 1/29 (3.4%)		
Gudas (2009)	OAT: 25 MF: 22	OAT: 5/25 (20%)‡ MF: 16/22 (73%)‡		OAT: 0/25 MF: 9/22 (32%) (7 OAT, 2 ACI)			
Horas (2003)	OAT: 20 ACI: 20	OAT: 4/20 (20%)§ ACI: 5/20 (25%)**		OAT: 0/20 ACI: 1/20 (OAT)		OAT: 2/20 (10%) ACI: 2/20 (10%)	OAT: 2/20 (10%) ACI: 0/20

MOS: mosaicplasty; OAT: osteochondral autologous transplantation; ACI: autologous chondrocyte implantation; MF: microfracture
* In this study, additional procedures were not reported separately by treatment group; among all 42 patients there were 3 with joint stiffness treated with manipulation under anesthesia (one of these required arthroscopy with loosening of adhesions to mobilize)
† Did not report on revisions or subsequent procedures
‡ For evaluation of cartilage repair
§ For limited flexion, drainage, resection of meniscus, unspecified
** For pain, ACL rupture, meniscopathy, valgus deviation, joint effusion

Table I 2a. Complications in nonrandomized comparative studies of osteochondral autograft transplantation

Author (year)	N	Site	Pain	Arthrofibrosis or joint stiffness	Donor site morbidity	Joint swelling/effusion	Subchondral cyst or geode on MRI	Arthrosynovitis on MRI
Derrett (2005)*	MOS: 20 ACI: 53	Knee						
Macarini (2003)	OAT: 15 ACI: 7 ACP: 40	Knee	OAT: 2/15 (13%) ACI: 2/7 (28.6%) ACP: 12/40			OAT: 3/15 (20%)† ACI: 3/3 (100%)† ACP: 0/40	OAT: 0/15 ACI: 0/3 ACP: 9/40	OAT: 0/15 ACI: 0/3 ACP: 28/40

			(30%)				(22.5%)	(70%)
Gobbi (2006)	OAT: 12 MF: 9 CP: 11	Talus	OAT: 2/12 (17%) MF: 1/9 (11%) CP: 1/11 (9%)	OAT: 2/12 (17%)	OAT: 0/12 MF: N/A CP: N/A			

MOS: mosaicplasty: OAT: osteochondral autologous transplantation; ACI: autologous chondrocyte implantation; MF: microfracture; CP: chondroplasty; ACP: abrasion chondroplasty
* Included an unknown number of patients from Bentley (2003)
† From MRI

Table I 2b. Revisions and re-operations in nonrandomized comparative studies of osteochondral autograft transplantation

Author (year)	N	Site	Arthroscopy	Revision or repeat of same procedure	Alternative cartilage repair procedure	Manipulation under anesthesia	Aspiration	Debridement (arthroscopic)
Derrett (2005) *	MOS: 20 ACI: 53	Knee	MOS: 6/20 (30%)† ACI: 19/53 (36%)†	MOS: 0/20 ACI: 1/53 (2%)	MOS: 1/20 (5%) (ACI) ACI: 0/20	MOS: 1/20 (5%) ACI: 8/53 (15%)	MOS: 1/20 (5%) ACI: 0/53	
Macarini (2003)	OAT: 15 ACI: 7 ACP: 40	Knee	OA: 0/15 ACI: 0/7 ACP: 7/40 (17.5%)‡					OA: 2/15 (13%) ACI: 0/7 ACP: 0/40
Gobbi (2006)	OAT: 12 MF: 9 CP: 11	Talus		OA: 0/12 MF: 0/9 CP: 1/11 (9%)				OA: 2/12 (16.6%) MF: 0/9 CP: 0/11

MOS: mosaicplasty: OAT: osteochondral autologous transplantation; ACI: autologous chondrocyte implantation; MF: microfracture; CP: chondroplasty; ACP: abrasion chondroplasty
* Included an unknown number of patients from Bentley (2003)
†"Unanticipated" arthroscopy, no indication described
‡ Follow-up for patients with persistent symptoms

Table I 3a. Complications, revisions, and re-operations in case series of osteochondral autografts: knee (n>30)

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
Infection							
Jakob (2002)	52	34 (14-66)	65	1 (2)	various sites in knee OCD, trauma, arthrosis	3 (2-4.5)	100
Karatiglis (2006)	36 (37)	32 (18-48)	64	1 (3)	femoral condyle, patellofemoral joint OCD, trauma, AVN	3 (1.5-6)	86
Solheim (2009)	69	33 (16-50)	59	3 (4)	femoral condyle, patella	7 (5-9)	
Hemarthrosis							
Chow (2004)	30	44l6 (19-66)	43	2 (7)	femoral condyle trauma, OCD, unknown	3.8 (2-5)	91
Jakob (2002)	52	34 (14-66)	65	1 (2)	various sites in knee OCD, trauma, arthrosis	3 (2-4.5)	100
Laprell (2001)	29	26	49	13 (45)	femoral condyle, patella OCD, trauma	8.1	83
Solheim (2009)	69	33 (16-50)	59	2 (3)	femoral condyle, patella	7 (5-9)	
Deep vein thrombosis							
Braun (2008)	33	34.3 (15-59)	70	1 (3)	femoral condyle OCD, traumatic, other	5.5 (3.6-8)	92
Karatiglis (2006)	36 (37)	32 (18-48)	64	1 (3)	femoral condyle, patellofemoral joint OCD, trauma, AVN	3 (1.5-6)	86
Solheim (2009)	69	33 (16-50)	59	1 (1.4)	femoral condyle, patella	7 (5-9)	
Osteoarthritis (radiograph) *							
Braun (2008)	33	34.3 (15-59)	70	17 (59)	femoral condyle OCD, traumatic, other	5.5 (3.6-8)	92
Barber (2006)	36	43 (17-69)	55	0	femoral condyle OCD, full-thickness defects	4 (2-7.4)	NR
Laprell (2001)	29	26	49	12 (41)	femoral condyle, patella OCD, trauma	8.1	83
Manipulation under							

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
anesthesia							
Jakob (2002)	52	34 (14-66)	65	1 (2)	various sites in knee OCD, trauma, arthrosis	3 (2-4.5)	100
Diagnostic arthroscopy							
Agneskircher (2002)	29	36 (16-60)	72	2 (7)	femoral condyle	1.5 (.25-4)	NR
Barber (2006)	36	43 (17-69)	55	14 (39)	femoral condyle OCD, full-thickness defects	4 (2-7.4)	NR
Chow (2004)	30	44l6 (19-66)	43	9 (30)	femoral condyle trauma, OCD, unknown	3.8 (2-5)	91
Jakob (2002)	52	34 (14-66)	65	6 (11)	various sites in knee OCD, trauma, arthrosis	3 (2-4.5)	100
Solheim (2009)	69	33 (16-50)	59	23 (33)	femoral condyle, patella	7 (5-9)	
Re-operation							
Agneskircher (2002)	29	36 (16-60)	72	1 (3)	femoral condyle	1.5 (.25-4)	NR
Chow (2004)	30	44l6 (19-66)	43	4 (13) †	femoral condyle trauma, OCD, unknown	3.8 (2-5)	91
Jakob (2002)	52	34 (14-66)	65	8 (15) ‡	various sites in knee	3 (2-4.5)	100
Karatiglis (2006)	36 (37)	32 (18-48)	64	9 (24) §	femoral condyle, patellofemoral joint OCD, trauma, AVN	3 (1.5-6)	86
Laprell (2001)	29	26	49	3 (10)	femoral condyle, patella OCD, trauma	8.1	83
Marcacci (2007)	27	29.3 (17-46)	73	3 (10) ††	femoral condyle	7	90
Solheim (2009)	69	33 (16-50)	59	19 (28) ‡‡	femoral condyle, patella	7 (5-9)	
Donor site morbidity§§							
Jakob (2002)	52	34 (14-66)	65	3 (6) §§	various sites in knee OCD, trauma, arthrosis	3 (2-4.5)	100
Laprell (2001)	29	26	49	5 (17)	femoral condyle, patella OCD, trauma	8.1	83
Marcacci (2007)	27	29.3 (17-46)	73	3 (10)	femoral condyle	7	90
Continuing pain							
Agneskircher (2002)	29	36 (16-60)	72	3 (10)	femoral condyle	1.5 (.25-4)	NR

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
Subchondral bone changes (edema or sclerosis on MRI)							
Marcacci (2007)	27	29.3 (17-46)	73	17 (71)	femoral condyle	7	90

OCD: osteochondritis dissecans; AVN: avascular necrosis

* new or progression of osteoarthritis
† 2 arthroscopic debridement of fibrocartilage, 2 total knee arthroplasty
‡ 2 plate removal, 1 mosaicplasty of contralateral knee, 1 scar revision, 4 revision grafting due to graft failure
§ 1 arthrolysis; 4 debridement and chondroplasty, 2 partial medial meniscectomy. 2 graft revision of loose grafts
** 3 high tibial osteotomies
†† 3 autologous chondrocyte implantation for failed grafts
‡‡ 1 arthroscopic synovectomy for septic arthritis, 10 debridements, 8 debridement + microfracture for new lesions or non-intact grafts
§§ pain while squatting and/or crepitation in donor joint

Table I 3b. Complications, revisions, and re-operations in case series of osteochondral autografts: ankle (n>30)

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
Infection							
Paul (2009)	112	32 (16-59)	65	3 (3)		4.5 (2-10)	NR
Donor site morbidity							
Baltzer (2005)	43	31.2	70	1 (2)	OCD, traumatic, arthritis	(0-4)	NR
Paul (2009)	112	32 (16-59)	65	10 (9)*		4.5 (2-10)	NR
Re-operation							
Baltzer (2005)	43	31.2	70	25 (58) †	OCD, traumatic, arthritis	(0-4)	NR
Kreuz (2006)	35	30.9 (18-44)	51	2 (6) ‡		4 (2.8-6.4)	NR
Scranton (2006)	50	36 (17-56)	57	17 (34)§		3 (2-7)	94%

OCD: osteochondritis dissecans
* poor Lysholm (<65) or WOMAC (>20) for donor knee

† Hardware removal
‡ 1 ACI following OATS failure; 1 revision OATS following graft necrosis
§ 10 arthroscopic debridement; 1 debridement of scar tissue; 4 screw removal; 2 revision OATS and subsequent arthrodesis due to severe degenerative changes

Table I 3c. Complications, revisions, and re-operations in case series of osteochondral autografts: multiple sites (n>30)

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
Infection							
Hangody (2008)	1097	NR	NR	4 (.4)	knee, ankle, shoulder, hip	NR	NR
Hemarthrosis							
Hangody (2008)	1097	NR	NR	56 (5)	knee, ankle, shoulder, hip	NR	NR
Deep vein thrombosis							
Hangody (2008)	1097	NR	NR	4 (.4)	knee, ankle, shoulder, hip	NR	NR
Degeneration at recipient or donor site							
Hangody (2008)	1097	NR	NR	17 (1.5)	knee, ankle, shoulder, hip	NR	NR
Diagnostic arthroscopy							
Hangody (2008)	1097	NR	NR	98 (9) *	knee, ankle, shoulder, hip	NR	NR
Donor site morbidity							
Hangody (2008)	1097	NR	NR	3% †	knee, ankle, shoulder, hip	NR	NR
Joint effusion (MRI)							
Link (2006)	55 (55)	34.5 ± 12.1	62	42 (76)	knee, ankle OCD, necrosis, other	0-3	NR
Bone marrow edema in/around grafts (MRI)							
Link (2006)	55 (55)	34.5 ± 12.11	62	28 (51) ‡ 5 (17) 2 (15)	knee, ankle OCD, necrosis, other	0-3	NR
Synovitis with joint effusion (MRI)							
Link (2006)	55 (55)	34.5 ± 12.1	62	40 (73) ‡ 10 (33) 3 (23)	knee, ankle OCD, necrosis, other	0-3	NR
Osteonecrosis in grafts (MRI)							
Link (2006)	55 (55)	34.5 ± 12.1	62	6 (11)	knee, ankle OCD, necrosis, other	0-3	NR

OCD: osteochondritis dissecans

* 31 for pain, swelling, or intraarticular bleeding; 26 for evaluation following new trauma; 41 evaluation for return to sporting activity
† Measured with Bandi scoring system incorporating pain and global assessment
‡ Findings at 3-11 months, 12-23 months, 24-36 months

Table I 4a. Complications and re-operations in nonrandomized studies of osteochondral allograft transplantation

Author (year)	N	Site	Arthroscopy	Alternative cartilage repair procedure	Debridement (arthroscopic)	Total knee arthroplasty
Pascual-Garrido (2009)*	OA: 16 ACI: 3 LBR: 9 ARIF: 15	Knee	OA: 0/16 ACI: 0/3 LBR: 0/9 ARIF: 15/15 (100%)‡	OA: 0/16 ACI: 1/3 (33%) (OA) LBR: 1/9 (11%) (MF) ARIF: 3/15 (20%) (OA, MF)		OA: 1/16 (6.3%)
Rue (2008)†	OA: 14 ACI: 15	Knee			OA: 1/14 (7%) ACI: 3/15 (20%)	

OA: osteochondral allograft; ACI: autologous chondrocyte implantation; LBR: loose-body removal; ARIF: arthroscopic reduction and internal fixation; MF: microfracture

***** Did not report on complications
† Reported no complications
‡ Hardware removal

Table I 4b. Complications, revisions, and re-operations in case series of osteochondral allografts: knee (n>20)
Case series using dowel-shaped grafts only

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
Infection							
LaPrade (2009)	23 (23)	30.9 (16-47)	56	1 (4)	14 OCD; femoral condyle	3 (1.9-4)	100
Osteoarthritis (radiograph)							
McCulloch (2007)	25 (25)	35 (17-49)	72	2 (8)	femoral condyle	3 (2-5.6)	100

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
Manipulation under anesthesia							
Williams (2007)	19 (19)	34 (19-49)	68	1 (5)	femoral condyle	4 (1.8-5.7)	NR
Re-operation							
McCulloch (2007)	25 (25)	35 (17-49)	72	1 (4)*	femoral condyle	3 (2-5.6)	100
Williams (2007)	19 (19)	34 (19-49)	68	5 (26)†	femoral condyle	4 (1.8-5.7)	NR
Diagnostic arthroscopy							
LaPrade (2009)	23 (23)	30.9 (16-47)	56	1 (4)	14 OCD; femoral condyle	3 (1.9-4)	100
Ligament reconstruction							
LaPrade (2009)	23 (23)	30.9 (16-47)	56	1 (4)	14 OCD; femoral condyle	3 (1.9-4)	100
Continuing pain							
McCulloch (2007)	25 (25)	35 (17-49)	72	1 (4)	femoral condyle	3 (2-5.6)	100

OCD: osteochondritis dissecans; SO: steroid-induced osteonecrosis
* Allograft fragmentation and removal followed by microfracture
† 1 second allograft procedure to correct surgical error; 2 revision allograft transplantation following graft collapse; 1 total knee arthroplasty; 1 autologous osteochondral transplantation following partial graft collapse

Table I 4c. Complications, revisions, and re-operations in case series of osteochondral allografts: knee (n>20)
Case series using dowel-shaped and geometric-shaped grafts

Outcome	No. patients (no. knees)	Mean age in years (range)	% male	No. knees (%) with complication	Etiology and location of chondral defect	Mean follow-up in years (range)	Percent follow-up
Hyperergic reaction							
Bakay (1998)	33 (33)	48 (21-64)	NR	1 (3)	various sites in knee	1.75 (.8-3.2)	NR
Osteoarthritis (radiograph)							
Emmerson (2007)	64 (66)	28.6 (15-54)	64	24/29 (83)*	OCD; femoral condyle	7.7 (2-22)	98
Subchondral cysts (radiograph)							
Emmerson (2007)	64 (66)	28.6 (15-54)	64	5/29 (17)	OCD; femoral condyle	7.7 (2-22)	98
Graft failure (radiograph)							
Bakay (1998) †	33 (33)	48 (21-64)	NR	8 (24)	various sites in knee	1.75 (.8-3.2)	NR
Görtz (2010) ‡	22 (28)	24.3 (16-44)	27	2/14 (14)	SO; femoral condyle	5.6 (2-19.6)	96
Re-operation							
Emmerson (2007)	64 (66)	28.6 (15-54)	64	10 (15) §	OCD; femoral condyle	7.7 (2-22)	98
Görtz (2010)	22 (28)	24.3 (16-44)	27	5 (18) **	SO; femoral condyle	5.6 (2-19.6)	96

OCD: osteochondritis dissecans; SO: steroid-induced osteonecrosis
* grade 1: n=7; grade 2: n=14; grade 3: n=10
† defined as sclerosis, narrowing or obliteration of joint space, or formation of osteophytes
‡ defined as resorption, collapse, or fragmentation of osseous portion of allograft
§ 5 revision allograft; 1 second allograft for additional lesion in same knee; 2 total knee arthroplasty; 1 unicompartmental knee arthroplasty; 1 graft removal
** 2 repeat allograft; 1 total knee arthroplasty; 1 partial meniscectomy; 1 arthroscopic debridement

Appendix J. Case Series – Data Abstraction

Table J1. Allograft case series (using dowel/cylinder/plug without hardware fixation)

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes				Complications
Studies with dowl-shaped allograft as primary/only type of graft used											
LaPrade (2009)	Case series IV Funding: none	Mean F/U: 3 years (range, 1.9 – 4 years) F/U rate: 100% (23/23)* *No patient was lost to follow up, however 3 patients did not have 2-year follow-up info. All 3 were college students who reported that their knees felt normal, and they did not want to return for the follow-up evaluation.	N = 23 patients (23 knees) 57% male (13/23) Mean age: 30.9 years (range, 16.4 – 46.9 years) **Patient characteristics** Previous surgery: 87% (20/23) (8 chondroplasty, 5 removal of loose body, 5 previous internal fixation, 4 microfracture, 4 subchondral drilling, 3 partial medial (and lateral) meniscectomy, 2 ACL reconstructions, 2 lateral retinacular release, and 5 others – screw removal, releases, debridements) Average age of implanted allografts: 20.3 days (range, 15-25 days)	**Inclusion:** • Refrigerated osteochondral allograft transplantation for the treatment of a symptomatic full-thickness articular cartilage defect of >3 cm^2 on the femoral condyles **Exclusion:** • NR	Etiology: 61% (14/23): localized osteochondral lesion due to a dislodged osteochondritis dissecans lesion of the femoral condyle 39% (9/23): localized full-thickness chondral defects **Total** • Mean defect size (cm^2): 4.8 (range, 3.1 – 9.6) • Number of plugs: 1 **Localization (n):** • 19 medial femoral condyle • 3 lateral femoral condyle • 1 both condyles	**Interventions:** • Treatment of focal articular cartilage defects of the femoral condyles with refrigerated osteoarticular grafts • A small medial or lateral parapatellar arthrotomy was performed, depending on the location of the defect **Co-interventions:** • Non-weight-bearing for 8 weeks • Quadriceps exercises and straight-leg raises with the patient wearing a knee immobilizer were performed 4 times daily • Low impact activities recommended for the first 12 months		Pre-op	Post-op	*P*-value	• 1- superficial cellulitis develop 2 weeks post-op • 5 surgical procedures were performed on 4 patients after graft implantation: -3 removal of symptomatic hardware from a concurrent proximal tibial opening-wedge osteotomy -1 underwent a diagnostic arthroscopy after sustaining a valgus twisting injury (also hardware removal) -1 lateral patellotibial ligament reconstruction for symptomatic medial patellar subluxation after a lateral release
							Modified Cincinnati knee-rating score				
							Symptoms	21.9 points	32.5 pts	p < 0.03	
							Function	27.3	36.5	p < 0.01	
							Mean	49.2	69	p < 0.02	
							IKDC	52	68.5	p < 0.03	
							Effusion rating*	A-1 B-17 C-2	A-20	p < 0.001	
							Passive extension*	A-7 B-11 C-2	A-9 B-9 C-2	NR	

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes	Complications
							Functional testing* | A-0 B-4 C-9 D-7 | NR | p < 0.001 *A (normal); B (nearly normal); C (abnormal); D (NR)	
McCulloch (2007)	Case series IV Funding: NR	Mean F/U: 35 months (range, 24–67 months) F/U rate: 100% (25/25)* *All 25 patients were available for assessment at a minimum of 2 years of follow-up	N = 25 patients (25 knees) 72% male (18/25) Mean age: 35 years (range, 17–49 years) **Patient characteristics** Previous surgery: 96% (24/25), including palliative or reparative measures as osteochondritis dissecans fixation, debridement, microfracture, and autologous chondrocyte implantation 13 (52%) were on workers' compensation Duration of symptoms: average interval from injury to surgery was 25 months (range, 3-70) Comorbidities: 56% (14/25) Classification: Co-existing abnormalities:	**Inclusion:** • Presence of a symptomatic full-thickness cartilage defect of at least 2 cm^2 **Exclusion:** • NR	Etiology: • 36% (9/25): degenerative • 32% (8/25): traumatic • 24% (6/25): osteochondritis dissecans • 8% (2/25): osteonecrosis **Total** • Mean primary lesion size (cm^2): 5.24 (range, 2.25–10.50) • Mean secondary lesion size (cm^2): 2.31 (range, 0.81-4.00) • Mean primary plug size (cm^2): 3.98 (range, 1.77-7.07) • Mean secondary plug size (cm^2): 1.80 (range, 0.64-3.14) • 5 patients had more than 1 lesion that required more than 1 graft to replace the damaged region - 1 had 1 plug on the medial and 1 lateral femoral condyle - 4 had 2 plugs on the same condyle because	**Interventions:** • A small arthrotomy and vastus sparing or lateral retinacular incision was used depending on the defect location • Associated procedures included 10 meniscal transplantations, 4 opening wedge high tibial osteotomies (HTOs), and 1 removal of previous osteotomy plate **Co-interventions:** • Patients remained touchdown weightbearing with the assistance crutches for 6 weeks • Progress was monitored by a physical therapist and were allowed unrestricted passive ROM	Objective Assessments Affected side | Unaffected side | Diff. (aff vs unaf) ROM (degrees) Pre-op: 123 | 129 | 6 Follow-up: 127 | 130 | 3 Difference (pre-op vs f/u): 4 (P = .774) | 1 (P = .434) Quad size (cm) Pre-op: 47.2 | 48.6 | 1.4 Follow-up: 46.2 | 47.6 | 1.4 Difference (pre-op vs f/u): -1 (P = .987) | -1 (P = .909) Subjective Scores Score*: Iso Allograft n=11 | Allo + MTx n=10 | Allo + HTO n=4 Lysholm Preoperative: 34 (±20) | 47 (±16) | 30 (±19) Follow-up: 60 (±26) | 68 (±22) | 82 (±2) P value: 0.008 | 0.013 | 0.0	**Outcomes (cont.)**: • Lysholm: 39 to 67, P < .0001 • IKDC: 29 to 58, P < .0001 • KOOS Pain: 43 to 73, P < .0001 • KOOS ODDS: 46 to 64, P = .001 • KOOS ADL function: 56 to 83, P < .001 • KOOS Sport and recreation function: 18 to 46, P < .001 • KOOS Knee related QOL: 22 to 50, P < .0001 • SF-12: 36 to 40, P = .014 **Complications:** • 2 (8%) total: • 1 was a failure secondary to allograft fragmentation • 1 had marked pain for greater than 6 months • No patients required further surgery as a result of either their osteotomy or their meniscal transplant

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes				Complications
					of the shape of the defect • Mean graft age on day of surgery: 24 days (range, 15-43) **<u>Localization (n/total):</u>** • Medial femoral condyle (17/25) • Lateral femoral condyle (7/25) • Both codyles (1/25)					02	
							IKDC				
							Preoperative	26 (±8)	36 (±14)	22 (±13)	
							Follow-up	59 (±23)	55 (±16)	62 (±10)	
							P value	0.003	0.017	0.003	
							KOOS Pain				
							Preoperative	40 (±15)	49 (±12)	38 (±15)	
							Follow-up	68 (±23)	75 (±19)	81 (±9)	
							P value	0.004	0.005	0.003	
							KOOS Symptom				
							Preoperative	43 (±21)	54 (±15)	36 (±28)	
							Follow-up	62 (±23)	63 (±19)	75 (±7)	
							P value	0.028	0.069	0.033	
							KOOS ADL				
							Preoperative	48 (±20)	70 (±17)	43 (±27)	
							Follow-up	78 (±21)	85 (±15)	90 (±4)	
							P value	0.004	0.028	0.013	
							KOOS Sport				

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes				Complications
							Preoperative	17 (±11)	20 (±16)	15 (±13)	
							Follow-up	50 (±34)	39 (±23)	54 (±20)	
							P value	0.007	0.032	0.018	
							KOOS QOL				
							Preoperative	24 (±18)	19 (±21)	22 (±13)	
							Follow-up	59 (±31)	41 (±19)	45 (±21)	
							P value	0.007	0.012	0.106	
							SF-12 PCS				
							Preoperative	38 (±8)	37 (±9)	29 (±5)	
							Follow-up	40 (±6)	42 (±8)	38 (±5)	
							P value	0.286	0.093	0.057	
							SF-12 MCS				
							Preoperative	53 (±14)	53 (±10)	43 (±9)	
							Follow-up	56 (±5)	57 (±6)	61 (±6)	
							P value	0.859	0.285	0.016	
							*MTx, meniscus transplantation HTO (high tibial osteotomy)				
Williams (2007)	Case series IV	Mean F/U: 48 months (range, 21–68	N = 19 patients (19 knees) 68% male (13/19) Mean age: 34 years (range,	**Inclusion:** • All patients had baseline preop	Etiology: -26% (5/19) full-thickness chondral	**Interventions:** • A limited knee arthrotomy (without	• Activities of Daily Living Score: o Pre: 56 ± 24 (range, 20-100) o Final f/u: 70 ± 22 (range, 30-				• No infections or deep venous thromboses • 1 required manipulation

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes	Complications
	Funding: none	months) F/U rate: 100% (19/19)* *minimum 2 years follow-up	19–49 years) **Patient characteristics** Previous surgery: 89% (17/19) (mean, 2 operations; range, 0-4) Including microfracture arthroplasty, mosaicplasty, meniscal repair, and others Duration of symptoms: 35 months (range, 4-122) Comorbidities: Classification: Co-existing abnormalities:	clinical outcome scores recorded in the database • Min. follow up of 2 years **Exclusion:** • Patients with multiple lesions, (non focal disease), ligamentous instability, or severe lower extremity malalignment	lesion -68% (13/19) osteochondritis dissecans -5% (1/19) osteonecrosis **Total** • Mean lesion size (mm^2): 602 (range, 121–1500) • Mean allograft storage time: 30 days (range, 17-42) • 47% (9/19) had concomitant procedures **Localization (n):** • All 19 grafts were placed on the femur: • 14 on medial femoral condyle • 5 on lateral femoral condyle	patellar eversion) was used to implant the allografts in the host femoral condyles • MRI scans were used to evaluate the morphologic characteristics of the implanted grafts **Co-interventions:** • Hinged knee brace and toe-touch weight-bearing for a min. of 8 weeks • A unicompartmental unloader brace was used for four months after the initial 8-week interval • Supervised rehab started 2 weeks post-op and continued for 4-8 months	98) o p < 0.05 • Combined SF-36 Score: o Pre: 51 ± 23 (range, 18-96) o Final f/u: 66 ± 24 (range, 9-96) o p < 0.005 • SF-36 Physical Component: o Pre: 32 ± 10 (range, 18-96) o Final f/u: 40 ± 12 (range, 22-59) o p < 0.005 • SF-36 Mental Component: o Pre: 46 ± 13 (range, 24-64) o Final f/u: 49 ± 11 (range, 38-62) o p = 0.1	of the knee while under anesthesia 2 months post-op • 1 underwent a second allograft 13 days post-op to correct a surgical error relating to poor graft-host match • 4 grafts failed clinically • After retrieval of the failed grafts, pathologic examination showed articular cartilage fragmentation and necrotic bone • At f/u of 48 months, 16/19 (84%) allografts still functioned within the host knee
Dowel/cylindrical-shaped allograft – but other types of grafting also used								
Bakay	Case series IV **Funding:** NR	Mean F/U: 19 months (range, 10 – 38 months) F/U rate: 100% (33/33)	N = 33 % male: NR Mean age: 48 years (range, 21 – 64 years) **Patient characteristics** Previous surgery: NR Duration of symptoms: NR Comorbidities: NR Classification: NR	**Inclusion:** • Age between 18 and 65 years • Unicompartemental disease • No other illnesses • Nearly full range of knee motion, normal muscle strength and intact join stability • Co-operation of the patient **Exclusion:**	Etiology: 55% (18/33) osteoarthritis/Post-traumatic OCD, (5/33) post-traumatic, (8/33) , osteoarthritis (2/33) **Total** • Mean defect size (cm): NR **Indications for resurfacing (n):** • Osteoarthritis/Post-traumatic oesteochondritis	**Interventions:** • 31 unicompartemental-unipolar resurfacings (94%) • 2 unicompartmental-bipolar resurfacings (6%) • 3 patellar replacements were combined with partial femoral condyle grafts were considered unicompartemental-unipolar resurfacings for the purposes of analysis. • One or two plugs used only. • Each graft 12mm or 17	• Bentley score (n) pre-op: • Excellent (0) • Good (0) • Fair (6) • Poor (27) • Bentley score (n) post-op: • Excellent (9) • Good (13) • Fair (6) • Poor (5) Overall success rate: 60%	• No sepsis or complications with wound healing. • One patient experienced a hyperergic reaction on the fifth postoperative day but recovered within two days on steroid and calcium derivative therapy.

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes	Complications
			Co-existing abnormalities: NR	• NR	dissecans (18) • Post-traumatic (5) • Post-traumatic chondromalacia (8) • Osteoarthritis (2) **Localization (n):** Whole tibial condyle replcemant (NR) Entire patellar surface (NR) **Number of plugs (n):** One or two	mm in diameter and the thickness of the cancellous bone was 1.5-2 cm. • The grafts were transplanted orthotopically and had the same size as the damaged surfaces which had previously been removed. • Cylindrical plug-shaped and mushroom-shaped allografts were press-fitted with no additional metal fixation, but we usually applied two malleolar AO lag screws for tibial plateau allografts. • In every instance, bone matrix gelatine (BMG) and fibrinsealant (Tissucol®, Immuno AG) were applied in thin layers. **Co-interventions:** • All patients had the same rehabilitation. • Continuous passive motion device was commenced immediately after the operation. • Weight-bearing allowed on the second post-op day. • Femoral and tibial replacements necessitated non-weight bearing for up to three months. • Active exercises start on the first post-op day and protective braces		

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes	Complications
						with a full range of motion were used in all patients for 4 weeks.		
Emmerson	Case series IV	Mean F/U: 7.7 years (range, 2-22 years) F/U rate: 98% (63/64)* *only one knee lost, 65 knees remaining for analysis	N = 64 (66 knees) 10% male (45/64) Mean age: 28.6 years (range, 15-54 years) **Patient characteristics** Previous surgery: • an average of 1.7 surgeries had been performed on each knee before the allografting procedure. • The most common prior surgery was arthroscopic loose body removal. Duration of symptoms: Comorbidities: Classification: Co-existing abnormalities:	**Inclusion:** • Undergone treatment of osteochondritis dissecans • Minimum 2 years follow-up **Exclusion:** • NR	Etiology 100% OCD **Total** • Mean defect size (cm): NR • Mean allograft size (cm^2): 7.5 **Localization (n/total):** • Medial femoral condyle (41/66) • Lateral femoral condyle (25/66) **Number of plugs/grafts (n):** NR	**Interventions:** • Donor/recipients matched solely on the basis of size using standard anteroposterior radiographs. • At the beginning of the study each graft was implanted within 5 to 7 days of procurement. • Later in the study, the procurement-use time period was extrened to a minimum of 14 days and a maximum of 28. (Allowing final bacterial cultures to be analyzed before implantation). • Full or mini-arthrotomy. • The area to be grafted was modified into a geometric shape, and the defect was prepared down to a depth of 2 to 10 mm. • For small and medium-sized lesions, a dowel techniquewas used • A shell allograft technique was used for larger lesions. **Co-interventions:** • Same rehabilitation for all patients • Use of continuous passive motion device during hospitalization	• Merle D'Aubigné and Postel scores 13.0 ± 1.7 preoperatively to 16.4 ± 2.0 at the most recent follow-up (P < .01). • 10 patients underwent reoperation after initial allografting procedure. • Kaplan-Meier survival analysis demonstrated 91% survivorship at 5 years (95% confidence interval, 83% to 99%) and 76% survivorship at both 10 and 15 years (95% confidence interval, 62% to 90% at both time points). • When patients were asked to subjectively compare their current knee function with that before allograft surgery, they had improved from a mean of 3.4 ± 1.9 to 8.4 ± 1.5 on a 10-point scale (P < .01)	• Ten patients (15%) underwent reoperation after the initial allografting procedure (Table 2). • Five of these patients underwent revision fresh osteochondral allografting at 1, 2, 6, 7, and 8 years. • One patient received a second oesteochondral allograft in the ipsilateral knee but at a site separate from the original OCD lesion. One patient was converted to a total knee arthroplasty 3 years postoperatively. • One patient underwent a revision fresh oesteochondral allograft at 5 years and then had a subsequent total knee arthroplasty performed 8 years after the index operation. • One patient underwent a unicompartmental knee arthroplasty after 5 years. • Lastly, 1 patient had the allograft arthroscopically removed at 7 years.

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes	Complications
						• Routine physical therapy with 3 months of protected weighbearing. • Closed-chain exercises at 4 weeks post-op and unrestricted daily living at 3 to 4 months.		
Görtz, Simon (2010)	Case series IV **Funding:** No commercial interests reported for all authors.	Mean F/U: 65.8 months (range 25-235 months) F/U rate: 100% (22/22) Surviving patients at end of study: 19 of 22.	N = 22 (28 knees) 27% male (6/22) Mean age: 24.3 years (range, 16-44 years) **Patient characteristics** Previous surgery: an average of 1.5 previous surgeries (range, 1-5 surgeries) • Arthroscopic debridement (7) • Drilling (4) • Loose body removal (4) • Bone grafting (3) • Distal femoral osteotomy (1) • No prior surgery (14) Duration of symptoms: NR Comorbidities: Sickle cell anemia (1), leukemia (9), systemic lupus erythematosus (5), Crohn's disease (2), Ulcerative colitis (6), closed head injury(1), Hodgkin's lymphoma(2), renal transplant (1), transient allergies(1), renal infection	**Inclusion:** • At least 2 years postoperative. • Received oesteochondral allografts for osteoarticular lesions sustained secondary to steroid associated osteonecrosis of the femoral condyles **Exclusion:** • NR	Etiology 100% OCD **Total** • Mean defect size (cm): NR • Mean total allograft surface area was 10.8 cm2 (range, 5.0–19.0 cm2 **Localization (n/total):** • Medial condyle (9/28) • Lateral condyle (6/28) • Medial and lateral condyle (12/28) **Number of grafts *(n):** • One (15) • Two (9) • Three (4) *plug and shell used **Type of grafts (n):** • Plug (9) • Shell (13)	**Interventions:** • The grafts were prepared to match the prepared lesion in size, shape, and depth. • After initial debridement, graft beds were prepared • down to healthy bleeding bone to a maximum depth of 12 mm. • The shell technique involves fashioning the graft and recipient site into complementary geometric shapes (trapezoidal) using burrs and hand tools. • More anterior lesions less than 30 mm in diameter (the maximum dimension of the available instruments) were treated with a round plug graft. • The plug technique involves preparation of the lesion site with a reaming tool placed over a guide wire and preparing a cylindrical graft using a coring device. **Co-interventions:** • All patients	• Mean IKDC pain score improved ($p<0.001$) from 7.1 to 2.0. • Mean IKDC function score increased ($p = 0.002$) from 3.5 to 8.3. • Merle D'Aubigné mean 18-point score improved ($p<0.001$) from 11.3 preoperatively to 15.8. • Mean Knee Society function score improved ($p = 0.005$) from 60.0 to 85.7 • 96% of patients avoided Arthroplasty.	• Two revision allografts at 45 and 40 months, respectively. • One conversion to total knee arthroplasty at 78 months

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics	Interventions and co-interventions	Outcomes	Complications
			(1), myositis (1) Classification: NR Co-existing abnormalities: NR			experienced the same rehabilitation. • Supervised ROM exercises and quadriceps strengthening. • Closed chain exercises such as cycling were begun by 1 month after surgery. • Weight bearing was limited to touch down for the first 6 weeks post-op followed by gradual increases. • Full weightbearing allowed at 3 months if radiographs showed evidence of osseous integration of the graft.		

DATA TABLES- AUTOGRAFT SAFETY: Study characteristics and demographics for OATS/mosaicplasty (autograft) case series studies evaluating safety - Series with >30 patients reporting safety outcomes)

Table J2: Knee (series with >30 patients reporting safety outcomes)

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics and treatment	Interventions	Complications, safety outcomes
Agneskirchner, Jens D (2001)	Case series* IV **Funding**: NR *(two	Mean F/U: 17.7 months (range, 3 – 46 months) F/U rate: 100% (29/29)	N = 29 (29 knees) 72% male (21/29) Mean age: 35.9 years (range, 16 – 60 years) PCT with screw fixation of the graft n = 12 58% male (7/12) Mean age: 31.2 years	**Inclusion:** • Grade 4 osteochondral defects with avital oesteochondral fragments. • Complaints for several years of load-dependent pain with reduction in walking	Etiology 100% OCD **Total** • Mean defect size (cm): 7.5 ± 4.1 (range, 4.0 – 20) * **Localization (n):**	Posterio condyle transfer (PCT) **Interventions: 2 series of pts** In the first series of 12 patients the procedure differed only by the use of an additional screw that was used to attach the graft to	• Three patients (10.3%) of the first series complained about persistent pain at follow-up and were not satistifed. • One arthrofibrosis after 6 months treated arthroscopically.

	series are described in this paper but are combined for many parts of the study)		(range, 21 – 43 years) Modified technique n = 17 82% male (14/17) Mean age: 39.2 years (range, 16 – 60 years) **Patient characteristics** Previous surgery: 72% (21/29) Previous surgery included mainly menisectomies, cartilage shaving and drilling. Duration of symptoms: "Several years"	distance. **Exclusion:** • NR	All in the patellofemoral joint • Medial femoral condyle (22) • Lateral femoral condyle (6) • Trochlea (1) *The paper did not report this average but instead included a table of individual patient data. From this data, a mean and a standard deviation were calculated in Microsoft Excel.	the femur from the articular surface. After that, the second series did not include the screw on the graft. • For correction of the varus malalignment in 13 patients a high tibial valgus osteotomy (HTO) was performed at the same time as the allograft procedure. • Five patients with deep osteonecrosis of more than 3 cm of subchondral bone received additional spongy plasty which was routinely taken from the tibial head. • Seven patients underwent additional oesteochondral transplantation at the patella or trochlea. • Two patients received a transplantation of autologous chondrocytes at the same time (OATS). **Co-interventions:** • All patients had the same rehabilitation. • Non-weight-bearing for six weeks. • Immediate continuous passive motion and muscular strengthening exercises starting the day after the drain removal.	No other complications reported. Lysholm score:
Barber (2006)	Case series IV **Funding:** NR	Average Time to F/U: 48 months (range, 24 to 89 months) F/U:	N = 36 Average age: 43 years (range, 17 to 69 years) 56% male (22/36) 20 right knees 16 left knees	**Inclusion:** • Outerbridge grade IV osteochondral lesions [10] • Large osteochondrosis dissecans with nonvital or loose fragments (A/B • Internationa	**Etiology** • Full-thickness defects, n =30; • Osteochondritis, n = 6. **Mean Defect size:** • Total 6.2 cm^2 (range, 2 to 10.5 cm^2; SD, 1.8); • PCT: 6.8 cm^2	Chondral osseous autrograft transplantation 100% **Interventions:** • COR system • Only 6mm diameter and 8mm depth plugs were used. **Cointerventions:**	Revisions Reoperations **Complications** 3 individuals had postoperative complications: • Muscle vein thrombosis • Effusion

				l Cartilage Research Society osteochondrosis dissecans Grade III and IV) • Focal osteonecrosis in the weight-bearing zone of the femoral condyle larger than approximately 4cm^2 • Osteochondral lesions that could not be addressed by standard osteochondral transfer techniques for other reasons (for example, depth) **Exclusion:** • Advanced osteoarthritis; • Significant narrowing of the joint lines and grade 2–4 osteoarthritic changes in more than the affected compartment. Deviation of the mechanical axis to the affected compartment	(range, 2 to 10.5 cm^2; SD, 1.9); • MegaOATS: 5.3 cm^2 (range, 3.1 to 7.1 cm^2; SD, 1.4). **Localization (n):** • Lateral femoral condyle (9) • Medial femoral condyle (27) **Number of grafts (n):** • 1 (15) • 2 (12) • 3 (6) • 4 (2) • 5 (1) • Average: 1.9 grafts • Average for patients with osteochondritis dissecans: 3.2 grafts ($P < 0.05$)	All patients had the same rehabilitation. • Immediate range of motion with a postoperative brace. • Non-weight bearing for the first 3 weeks postoperatively. • Progression weight bearing was allowed between 3 and 6 weeks, full weight bearing after that.	after tumbling • Inflammation of skin incision **Safety outcomes** **Subjective satisfaction** • Patients stated overall improvement of knee function of an average 89% (range, 70% to 100%; SD, 10.7), on a scale with 0% being knee function not allowing one to participate in normal daily-life activities and 100% representing a knee function that allowed the patient all activities, including sports, without any limitations at the same level as before the injury. • Two patients did not subjectively benefit from surgery and were subjectively not satisfied with their outcome. **Lysholm score** Average score preop: 44 Average score at follow-up: 84 Tegner activity scale average score at follow-up: 5 Repeat arthroscopy was performed in 14 patients and showed good incorporation of

							the grafts in all cases. No patients showed sclerotic or cystic changes or joint-line narrowing in radiographic examinations performed at follow-up.
Braun (2008)	Case series IV **Funding**: author SB is currently working as a research fellow at a nonprofit research foundation in the USA. Arthrex Inc. (Naples, FL, USA) is financially supporting this research position. There was no financial support or funding for this study. The remaining authors declare	Mean F/U: • Total: 66.4 months (range, 46 to 98 months; SD, 13.2); • PCT group: 77 months (range, 62 to 98 months; SD, 9.3); • MegaOATS group: 55.2 months (range, 46 to 62 months; SD, 4.9). F/U rate: 33/36 patients (91.6%)	N = 36 (36 knees) % male (/) Mean age: years (range, years) **Previous surgery:** Patients having had surgery previously: 24 (73% (out of 33 patients)) Average number of prior surgeries: Total: Previous surgeries included: • Arthroscopy • Removal of loose bodies • Cartilage smoothening • Meniscal surgery • Drilling of osteochondrosis dissecans • Refixation of osteochondrosis dissecans • Anterior cruciate ligament reconstruction • Foreign body removal • Distal patella realignment • Bone biopsy • Cancellous bone grafting • Removal of bursa • Open	**Inclusion:** • Outerbridge grade IV osteochondral lesions [10] • Large osteochondrosis dissecans with nonvital or loose fragments (A/B • International Cartilage Research Society osteochondrosis dissecans Grade III and IV) • Focal osteonecrosis in the weight-bearing zone of the femoral condyle larger than approximately 4cm^2 • Osteochondral lesions that could not be addressed by standard osteochondral transfer techniques for other reasons (for example, depth) **Exclusion:** • Advanced osteoarthritis; • Significant narrowing of the joint lines and grade 2–4 osteoarthritic changes	**Etiology** • Trauma, n = 9 (27%) • Osteochondritis, n = 18 (55%); • Osteonecrosis, n = 2 (6%); • Defects after meniscal surgery n =2 (6%); • Idiopathic after multiple surgeries n = 2 (6%). **Mean Defect size:** • Total 6.2 cm^2 (range, 2 to 10.5 cm^2; SD, 1.8); • PCT: 6.8 cm^2 (range, 2 to 10.5 cm^2; SD, 1.9); • MegaOATS: 5.3 cm^2 (range, 3.1 to 7.1 cm^2; SD, 1.4). **Localization (n):** • Lateral femoral condyle (6) • Lateral femoral condyle (27)	MegaOATS, n = 17 PCT, n= 16 **Interventions:** MegaOATS is noted to be a further development of the transfer of the posterior condyle, • Press-fit of osteochondral transfer plus with the transfer of the posterior femoral condyle • In a few cases with an osteochondral defect far posterior close to the osteotomy, there was not sufficient bone support for press-fit fixation. A fixation of the graft with a minifragment screw in the previously described fashion was therefore necessary. **Additional procedures(n):** • Re-correction of tibial tuberosity • Removal of bone spurs • HTO (high tibial osteotomy) • OATS lateral femoral condyle (in patients also receiving PCT) • OATS trochlea • Cancellous bone grafting • Patella realignment distal and soft tissue;	Revisions/failures NR **Complications** 3 individuals had postoperative complications: • Muscle vein thrombosis • Effusion after tumbling • Inflammation of skin incision **Safety outcomes** **Subjective satisfaction** • Patients stated overall improvement of knee function of an average 89% (range, 70% to 100%; SD, 10.7), on a scale with 0% being knee function not allowing one to participate in normal daily-life activities and 100% representing a knee function that allowed the patient all activities, including sports, without any limitations at the same level as before the injury. • Two patients did not subjectively benefit

	that they have no competing interests.		reduction and internal fixation of fracture of distal femur with join fracture • Removal of bone cyst	in more than the affected compartment. Deviation of the mechanical axis to the affected compartment		• Partial menisectomy • Revision ACL reconstruction • Autologous chondryte implantation **Cointerventions:** All patients had the same rehabilitation. • 6 weeks of nonweight-bearing on crustches and limited flexion up to 90°. • Continuous passive motion for at least 4 hours/day. • Full weight-bearing and a free range of motion were allowed 10 weeks postoperatively. • Comeback to recreation sports was allowed 6 to 9 months after surgery.	from surgery and were subjectively not satisfied with their outcome. **Lysholm score** Average score preop: 49.52 points, SD 17.805 (range, 12 to 79) Average score at 66.4 months: 81.88 points, SD 16.772 (range, 40 to 100)
Chow (2004)	Case series IV **Funding:** NR	Mean F/U: 45.1 months (range, 24 to 63 months). F/U rate: 90.9% (30/33)	N = 33 (# knees) 43% male (13/30) Mean age: 44.6 years (range, 19 to 66 years) **Symptom duration:** 1 month to 15 years (median, 9.5 months). **Previous surgery:** Ten total, 1 lateral and 4 medial partial meniscectomies, 2 chondroplasties (drilling and abrasion arthroplasty), 1 OCD fixation, and 2 diagnostic arthroscopies.	**Inclusion:** • Full-thickness chondral and osteochondral defects demonstrated by arthroscopy, • Defect location at the medial or lateralfemoral condyle, • Dimensions ranging from 1 to 2.5cm of defect diameter, and • Radiographic evidence of physeal closure of the distal femur and the proximal tibia. **Exclusion:** • Associated	Etiology Trauma, n= 17 (%) Osteochondritis dissecans, n = 4 Unknown, n = 9 Mean defect size (cm^2): NR Mean number of grafts: 2.2 (range, 1 to 4) Localization, n patients (%): Lateral femoral condyle, n = 28 (93.3%) Medial femoral condyle, n = 2 (6.7%)	**Autogenous Osteochondral Transplanation** **Interventions:** • The COR-System (Mitek Products, Westwood, MA) was used in this study. • The diameter of the graft harvester is 6 mm with a depth stop at 8 mm. Thus, grafts of standard diameter (6 mm) and length (8 mm) can be achieved. • An open technique may be used if arthroscopic access to the defect is difficult. • Loose fragments are removed from the defect site with a shaver or a curette until the margins of	Complications: Postoperatively, 2 patients developed a painful hematoma and aspiration of the knee joint was performed. Reoperations Graft biopsies were performed in all patients undergoing second-look arthroscopy. Histologic examination of the autogenous osteochondral plugs revealed normal hyaline cartilage in 7 of 9 patients and degenerative cartilage in 2. Revisions

				tibial or patellar articular cartilage defects, • generalized osteoarthritic changes of the knee joint, • Osteophyte formation in the intercondylar notch area, • Mechanical axis malalignment with abnormal orientation of the knee joint, • Presence of a collagen disease, and • Skeletal immaturity. • Neither meniscal tears nor anterior cruciate ligament (ACL) disruptions were contraindications for the procedure.		the defect are well defined. • Drilling is performed to the subchondral bone up to a depth of 8 mm. All holes may be drilled at once, maintaining a 1- to 2-mm bone bridge between recipient sites to achieve a tight press-fit. • If the level of the graft is higher than the surrounding bone, a tamp is inserted into the joint over the graft core. • **Cointerventions:** All patients had the same rehabilitation. • Patients remain non–weight-bearing for 3 weeks, while active knee motion is encouraged. • During the next 3 to 6 weeks, the patient is allowed partial weight bearing. • Light running is permitted when the patient regains full range of motion and shows no signs of effusion, usually at 12 weeks.	Failures 2 patients underwent a total knee replacement 39 and 47 months after the AOT. Safety outcomes **Mean Lysholm Score:** Preo op, 43.6 (range, 18-61) Post-op, 87.5 (range, 57-100), which was statistically significant compared with the preoperative mean value ($P > 0.001$, paired t test). **Outcome score** • Twenty-five patients (83.3%) had an excellent or good outcome. • Three patients (10%) had a fair result • 2 (6.7%) had a poor result. **IKDC evaluation Form** **Pre-op:** • 19 knees (63.3%) severely abnormal • 11 knees (36.7%) as abnormal. **Post-op** • 8 knees (26.7%) normal • 18 knees (60%) near normal • 2 knees (6.7%) as abnormal • 2 knees (6.7%) severely abnormal.
Jakob (2002)		Mean F/U: 37 months (range, 24-56 months)	N = 52 (59 knees) % male (34/52) Mean age: 34 years	**Inclusion:** •	**Etiology** Osteochondritis dissecans, total n = 13	Mosaicplasty **Interventions:**	**Reoperations** Second-look arthroscopies in 10

		F/U rate: 100% Postoperative follow-up at 4, 8, 12, 24 and 52 weeks.	(range, 14 to 66 years) **Previous surgery:**	**Exclusion:** •	• OCD of the medial condyle, n =8 • OCD of the lateral condyle, n =4 • OCD of the patella, n =1 Acute trauma, n =5 Posttraumatic lesions of the femoraltibial joint, n = 16 Femoropatellar arthrosis, n = 10 Femoropatellar maltracking, n = 5 Localized degeneration, n =3 **Mean defect size (cm^2):** 4.9 (range, 1.5 to 16.0) **Size (diameter range in cm), n patients** Small (<2.0), n = 13 Intermediate (2.0 to 2.9), n = 25 Large (≥3.0), n = 14 **Number of patients with contralateral donor site**, n =7 **Average number of plugs:** 6 (range, 1 to 16)	• All procedures but two done with open arthrotomy. • Two exception non-arthrotomy procedures were done with arthroscopy. • In 22 of 52 patients (42%), mosaicplasty was done without any supplementary procedures. • Small cylindrical osteochondral plugs (4.6-7.4mm diameter; 2-3cm length) were retrieved from nonweightbearing regions of the ipsilateral or contralateral knee and implanted into corresponding holes of the well-prepared defect (which previous had debridement). • The use of plugs taken from the contralateral knee was necessary in four patients with distinct femoropatellar arthrosis • Defect size was determined by analysis of preoperative MRI scan. • Gernerally, 70% to 80% coverage of the defect was achieved. • SDS soft delivery system was used for less traumatic explantation or implantation of plugs. • Supplementary surgical procedures • Correction of femoropatellar malalignment, n = 29 • Correction of femorotibial malalignment, n = 7;	patients (4 to 41 months postoperatively) **Failures/Revisions** Reoperation because of graft failure, n = 4 **Safety outcomes** International Cartilage Repair Society Classification Subjective status of the treated join as compared with the contralateral knee

						• Reconstruction of anterior cruciate ligament, n = 5; • Partial medial menisectomy, n =3; • Surture of meniscal tear, n = 1; • Reconstruction of lateral collateral ligament, n = 1; • Total synovectomy, n = 1. **Cointerventions:** All patients had the same rehabilitation. • Average hospital stay was 10 days (range, 6-21 days). • Continuous passive motion was instituted on the second day after surgery. • During the first 3 postoeprative weeks, patients were allowed 100° knee flexion; afterward the ROM was unrestricted. • Depending on the size of the defect (smaller or larger than 4cm^2), only partial weight bearing activity (max, 15-25 kg) was recommended for 4 to 8 weeks.	
Karataglis (2006)	Case series IV **Funding**: NR	Mean F/U: 36.9 months (range: 18–73 months) F/U rate: 85.7% (36/42 patients)	N = 36 (37 knees) 64% male (23/36) Mean age: 31.9 years (range: 18–48 years) **Previous surgery:** NR	**Inclusion:** • NR **Exclusion:** • NR	Etiology • Osteochondritis dissecans (OCD) in 10 cases; • Avascular necrosis (AVN) in 2, • Lateral patellar maltracking in 7, • 17 patients, the defect was post-traumatic following a road traffic accident, fall from a	OATS **Interventions:** • Grafts were harvested from the lateral or medial edge of the trochlea and secondarily from the notch if more graft was required. • In 22 cases, graft harvesting and subsequent implantation was carried out following anathrotomy,	9 patients had a second look arthroscopy for ongoing swelling, pain or clicking 7-13 months following their initial procedure. • Arthrolysis, n=1 • Debridement and Chondroplasty, n =4

					height or a sporting injury. **Mean defect size (cm):** 2.73 cm^2 (range, 0.8-12) **Localization:** • Medial femoral condyle, n = 18 cases; • Lateral femoral condyle, n = 8; • Trochlea, n =7; • Patella, n = 4.	while in the remaining 15 cases, grafts were harvest through miniarthrotomy and implanted arthroscopically. **Concomitant interventions:** • ACL reconstruction, n =4 • Lateral meniscal repair, n = 1 • Lateral release or an Elmslie-Trillat procedure in all 7 cases with an element of lateral patellar maltracking. **Cointerventions:** All patients had the same rehabilitation. • Drain inserted into the joint for 24 hours • Passive mobilization of the knee as soon as pain allowed • Touch-toe weight bearing was advocated for 4-6 weeks postoperatively with gradual progression to full weight bearing. • Patients who underwent osteochondral transplation to the articular surgace of the trochlea or the patella had their knee immobilized in extension for 3-4 weeks in order to protect the graft.	• Partial medial Meniscectomy, n = 2 • Graft revision, n=2 Minor complications such as deep vein thrombosis and one superficial wound infection cleared up with oral antibiotics. **Safety outcomes** **Tegner activity scale** Postoperative score average: 3.76 (range, 1-8) Postoperative score average NR **ADL scale on the Knee Outcome Survery** Average score preoperatively: 72.3 (18 to 98)
Laprell	Case series IV **Funding:** NR	Mean F/U: 8.1 years (range, 6 to 12 years) F/U rate: 100%	N = 35 49% male (17/35) Average age: 26 years (range, NR)	**Inclusion**: • Radiological and arthroscopic proof of an oesteochondral defect with an unstable dissecate. • Presence of clinical symptoms such as load-dependent pain, recurrent swelling or blocking.	Etiology Osterochondrosis dissecans, n= 27 (%) Posttraumatic osteochondral defects, n= 8 (%) **Mean defect size:** NR **Localization (n):**	OATS autograft • Grafts were harvest with a diamond bone cutter from the posterior part of the medial or lateral femoral condyle. • All patients underwent MRI and routine arthroscopy shortly before the osteochondral	**Revisions** 31 pateints underwent a resarthroscopy between the 12 and 20 weeks postoperatively. **Failures** NR. **Safety outcomes** • Standard

				• Severe impairment in daily living activites. • In case of osteochondritis dissecans, closed epithphyseal plates. **Exclusion:** NR	• Lateral part of the medial femoral condyle, n =29 • Lateral femoral condyle, n =3 • Patella, n =3 (%)	transplantation. • Doral approach through the popliteal fossa was performed to harvest the grafts from the posterior part of the femoral condyles. • One graft was harvested per each femoral condyle (i.e., if two, then both knees were harvested from) • Cylinder sizes varied between 11 and 23 mm (average diameter 15.6 mm) • Press-fit implantation under manual pressure. **Cointerventions:** • Continuous passive motion on the first postoperative day. • Partial weight bearing with 20kg was allowed within the 1st week of surgert. • Hospital stay varied between 13 and 22 days • After discharge, patients continued with partial weight-bearing for 6-8 weeks.	cartilage evaluation form • 12 patients were graded as normal (grade 1) • 14 knees were nearly normal (grade II) • 3 were abnormal (grade III) • No patients were assessed as severely abnormal (grade IV) **Activity level*** From ICRS form Preinjury levels (n) • I (2) • II (10) • III (14) • IV (3) Preopertively (n) • I (0) • II (0) • III (6) • IV (23) Postoperatively (n) • I (0) • II (3) • III (20) • IV (6) **Kellegren and Lawrence** Preoperative grades (n) • 0 (19) • I (6) • II (4) • III (0) • IV (0) Postoperative grades (n) • 0 (9) • I (14) • II (6) • III (0)

							• IV (0) **Complications** • In 16 patients numbness in a small area lateral of the anterior arthrotomy probably caused by injury of infrapatellar nerve was observed. • Hemarthrosis was aspirated in 13 patients. 12 patients developed new radiological signs of osteoarthrosis with a decrease in the radiological score of Kellgren and Lawrence by about one stage.
Maracacci (2007)	Case series IV **Funding:** NR	Minimum F/U: 2 and 7 years. F/U rate: 100% (not including the 3 failures which resulted in reoperation)	N = 30 (knees) 73% male (22/30 patients) Mean age: 29.3 years (range, 17-46 years). **Previous surgeries (n):** • Meniscectomies (6) • ACT reconstructions (7) • Shaving of chondral lesions (2) • Removal of a loose body (1) • No previous surgery (17)	**Inclusion:** • Patients aged 16 to 50 years, • Clinical symptoms such as knee pain or swelling, • Grade III to IV chondral lesions of the femoral condyles of 1.0 to 2.5 cm^2. **Exclusion:** • Chondral lesions larger than 2.5 cm^2 or smaller than 1.0 cm^2. • Noncorrected axial deviation or knee instability	Etiology 100% cartilage grade II to IV lesion of the weight bearing surface of medial or lateral femoral condyle less than 2.5cm^2 Mean defect size (cm): NR Localization (n): • Medial femoral condyle (17) • Lateral femoral condyle (13) Number of plugs: NR	All patients were treated with mosaicplasty **Interventions:** • All surgeries were performed by arthroscopy. **Concomitant interventions (n):** • ACT reconstructions (9) • Meniscectomies (13) • Medial collateral ligament repair (1) **Cointerventions:** All patients had the same rehabilitation. • Nonweightbearing with complete range of motion for the first postoperative month. • Gradual reintroduction to walking with full weighbearing. • During the first 3 months after surgery, patients followed a	**Failures** Three patients with failed results at early stage (around 18 months) were retreated by autologous chondryte implantation. Safety outcomes IKDC objective At 2-year follow-up • A (11) • B (12) • C (4) • D (3) At 7-year follow-up • A (7) • B (16) • C (4) • D (3) IKDC subjective Preoperative average ± SD: 34.8 ± 13.5 7 –year follow up

						progressive strengthening program to recover leg-muscle strength. • Full athletic activity was permitted after 4 months (contact and traumatic sports were allowed after 6 months), and return to sports at the preoperative level was usually attempted after 6 to 8 months.	average ± SD: 71.7 ± 18.8 ($P < 0.0005$). Tegner activity score
Solheim (2009)	Case series IV **Funding:** No conflicts of interest.	Mean F/U: months (range, months) F/U rate: 95% (69/73)	N = 73 (73 knees) 59% male (41/69) Median age: 33 years (range, 16-50 years) Median symptom duration: 60 months (range, 1 month to 30 years) **Previous surgery:** NR	**Inclusion:** • 50 years or younger; • Symptomatic focal full-thickness chondral lesions verified by arthroscopic examination. **Exclusion:** • Joint space narrowing (<4mm); • Axial malpositioning; • Ligament instability; • Inability to follow the rehabilitation protocol.	Etiology 100% OCD Median defect size (cm): $3cm^2$. Localization (n): • Medial femoral condyle (n=40), • Patella (n=18), • Lateral • Femoral condyle (n=7) • Trochlea (n=4)	Mosiacplasty **Interventions:** • After arthroscopic evaluation a mosaicplasty procedure was performed as described by Hangody et al. • The lesion was debrided and measured. • Grafts were harvested from the periphery of the femoral condyles at the level of the patellofemoral joint and transplanted to corresponding burr holes in the defect. • Usually the procedure was performed using a mini-arthrotomy. • In small defects of the femoral condyle an arthroscopic approach was used. In lesions of the patellofemoral joint a large arthrotomy with luxation of the patella was used. **Cointerventions:** All patients had the same rehabilitation. • Continuous passive motion for length of stay at the hospital (minimum 4 days) • Use of crutches for at least 6 weeks • Full weight	**Revisions** Second look arthroscopy due to insufficient improvement of symptoms, n= 23 from 1 to 5 years post-mosiacplasty. **Safety outcomes** (At preop, 1 year and 5-9 years) **Lysholm scores (0 = not satisfied, 100 = completely satisfied)** • Pre-op: 62 • Post-op (12 month follow-up): 24 **VAS – Pain (0 = no pain, 100 = worst possible pain)** • Pre-op: 48 • Post-op (12-month follow-up): 81 **Mean degree of satisfaction** with the outcome was 70 (DC 28) and 61 patients (88%) stated that they would have undergone the surgery again.

						bearing was then introduced gradually.	

Table J3: Talus (ankle) and other anatomic sites (series with >30 patients reporting safety outcomes)

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics and treatment	Intervention	Complications/safety outcomes
Talus							
Baltzer (2005)	Case series LoE: IV Funding: NR	Follow-up: 100% Mean time to F/U: >2 years (max 4.5 years) Follow up examinations at: 3 months 6 months 9 months 12 months Every following year (max 4.5 years)	N = 43 70% male (30/43) Mean age: 31.2 years Symptom duration: >9 months before surgery.	Inclusion: Traumatic and nontraumatic osteochondral defects (OCD, traumatic lesions and focal osteoarthritis) Chondral or osteochondral defects of the talus (Outerbridge stage III and IV) to a maximum of 4 cm^2 Age greater than 14 and less than 55 years Orthograde weight bearing Stable ligaments of the ankle joint, Absence of severe knee pain or injury in the past. Exclusion: General osteoarthritis or instability of the anke joint, Deviation in the axis of the leg, Young than 14 and older than 55 years, Sever chondral of osteochondraf defects larger than 4cm^2, Osteoarthritis of the knee joint.	Etiology Osteochondritis dissecans stage II-IV, n =22 Post-traumatic cartilage defects, n =16 Focal osteoarthritis, n =5 Localization (n): All grafts were placed in the talus. Medial dome of the talus, n =27 (62%) Central dome, n =2 (5%) Lateral dome, n =14 (33%) Mean size of defect: 1.7 cm^2 (maximum, 3.7cm^2) Mean number of grafts: 1.8 (max 4)	Intervention: Diagnostic arthroscopy Anteromedial or antrolateral arthrotomy (23 cases) Medial malleolar osteotomy (30 cases) of the distal tibia were performed. Autograft culinders harvest from the upper lateral condyle of the ipsilateral knee, Depending on the size of the defects the transplantation were either implanted using a single donor or the mosaicplasty OATS was used for transplantation. Concomitant interventions: Cointerventions:	Failures/Revisions NR Safety outcomes Return to Sports after hardware removal and/or second-look arthroscopy at approximately 9 months. VAS – pain (0 to 10 with ten being the worst imaginable pain) Pre-op: 4.4 6 months: 2.3 1 year: 1.6 2 years: 1.1 Subjective score after surgery (would they do it all over again?) mean scale value, 2.2 with 1 being full ROM and pain free on a scale from 1 to 6. Evanski and Waugh score Pre-op: 52 6 months: 88 (improved, out of 100 possible points) Score described by Mazur et al Pre-op: 53 6 months: 90 (improved, out of 100 possible points) ROM (range of motion) In the group of patients who

							received 1 osteochondral cylinder (n = 15), all 8 patients with a follow-up of 12 months reached nearly the full ROM of the contralateral site Patients who received 2 osteochondral cylinders (n = 20) did better in the early follow- up but needed longer (>24 months) to gain full ROM. Of the group of 4 patients receiving 3 osteochondral cylinders (n = 8), none finally reached full ROM .
Scranton (2006)	Case series IV **Funding:** No conflicts of interest	Mean F/U: 36 months (range, 24 to 83 months) F/U rate: 100% (50/50)	N = 50 (50 knees) 60% male (30/50) Mean age: 35 years (range, 17 to 56 years) **Symptom duration:** • Symptoms for more than one year before the diagnosis of an osteochondral lesion, n = 40 (80%) • Less than one year, n =10 (20%) **Previous surgery:** 64% of patients had undergone previous ankle surgeries including: • Arthroscopic or open debridement • Curettage • Drilling • Internal fixation • Grafting	**Inclusion:** • Type-V lesions treated by an osteochondral autograft from the ipsilateral knee • Cystic lesion between 8mm and 20 mm in diatmeter **Exclusion:** • Larger lesions in which allograft plugs or en bloc allografts were used	Etiology 100% type-V cystic osteochondral lesions of the talus Defect size range: 8mm to 20mm in diamter Localization (n): • Talus (n =50, 100%)	OATS for all patients **Intervention:** • Impingement spurs or loose bodies were removed • Release of anterior talofibular ligament or Anterior subluxation Forced plantar flexion • Anterior medial ankle arthrotomy • Medial malleolus is predrilled with 0.53mm pins and over-drilled with an AO Synthes 2.7 mm cannulated drilled to a depth that crosses into the tibial plafond. • The damaged surface of the talus is debrided. • The cystic lesion is drilled perpendicularly. • Graft taken from knee through arthroscopy. • The graft is is introduced into the talar hole in optimal oreientation for	Revisions Reoperations Failures Further surgery required in 17 patients: **Safety outcomes** **Karlsson-Peterson Ankle Scoring method** • 90% of patients were satisfied with outcome • Mean score at pre-op: 30.3 (range, 52 to 90) • Mean score at final F/U: 76.2 (range, 5 to 100) • Ankle stiffness, mean score: 3.2 out of 5.0 (2 to 5). • Mean pain score: 14.2 out of 20 (0 to 20)

						articular congruity and until it is flush with the articular surface. • The medial malleolus is replaced and fixed with two 40mm cannulated 4.0 mm-diameter cancellous AO screws. **Concomitant interventions:** • Malloelar osteotomy, n =26 (52%) **Cointerventions:** • All patients had the same rehabilitation. • Non weight bearing in a bootwalker for 3 weeks. After 6 weeks full weight-bearing is allowed.	
VARIOUS SITES							
Hangody (2008)	Case-series LoE: IV Funding: none	F/U: NR	N = 1097 (789 femoral condyles, 147 patellofemoral joint 31 tibia condyles, 98 talar domes, 8 capitulum humeri, 3 humeral heads, 11 femoral heads) Age: NR Sex: NR Subgroup*: 93 pro athletes (51 medial condylar, 15 lateral condylar,	NR Cases reported between February 6, 1992 – August 31, 2006	N = 1097 (incl. pro athletes):	Autologous osteochondral grafting: mosaicplasties Subgroup (413 patients): 3 techniques providing fibrocartilage repair: -Pridie drilling -Abrasion arthroplasty -Microfracture Compared to	N = 1097: -4 deep infections -56 painful haemarthroses -4 minor thromboembolic complications • -No complications with pro atheltes

			1 lateral tibial condylar, 10 patellofemoral, 14 talar, 2 capitellum humeri) Age: 26 (14-39) yrs Sex: m:f 55:38 *may or may not be included in the 1097 (?) Subgroup: 413 patients (4 arthroscopic resurfacing techniques compared in a multicentric, prospective study) Subgroup*: -126 mosaicplasties with greater than 3 years F/U -113/126 (90%) F/U -2/3 had full-thickness cartilage defects -1/3 had osteochondral destructions *may or may not be included in the 1097 (?) Subgroup: -36 patients with talar implantations -F/U: 4.2 yrs (2-7 yrs) -Age: 27 (16-47) yrs			hyaline cartilage repair: -Mosaicplasty	
Link	Case series LoE: IV Funding: NR	F/U: All patients examined within one year of surgery, n = 30	N = 55 Mean age: 34.5±12.1 years 62% male (34/55)	Inclusion: NR Exclusion:	Etiology, n patients (%) Osteochondritis, dissecans, n = 12 Osteonecrosis, n = 5	OATS Intervention: All grafts in this	Failures 6 patients with complete or partial osteonecrosis.

		second exam at 12-24 months and n = 13 with 25-36 months postoperatively. 100% follow-up within one year.	Symptom duration: NR Previous surgery: NR	NR	Osteochondral defects, n = 38 Localization (n): Knee joint (45) Ankle joint (10) Mean defect size: Number of grafts (n): Mean, 1.9, range 1-5 cylinders	series were harvested from the knee joints; the donor site was the non-weight-bearing femoral condyle distant from the patella –femoral joint surface; MR imaging Concomitant interventions: NR Cointerventions: NR	Revisions/reoperations NR Safety Outcomes Modified Lysholm Score (no scores reported)

Table J4: Series designed specifically to evaluate adverse events or safety outcomes regardless of number of patients.

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics and treatment	Intervention	Complications/safety outcomes
Paul (2009)	Case-series LoE: IV (therapeutic) Funding: none Designed to evaluate DONOR SITE MORBIDITY	F/U: 36 months (range, 1-124 months) 112/200 (56%) F/U for ≥ 2 yrs Avg: 55 mo (range, 25-124 months)	N = 200 patients Age: 32 ± 10 years (range, 14-57 yrs) Sex: 123 men, 77 women N = 112 (2 yr F/U) Age: 32 ± 9 years (range, 16-57 yrs) Sex: 73 men, 39 women	Inclusion: -autologous osteochondral transplantation to treat a cartilage defect of the talus -asymptomatic knee to serve as the donor site	-72 (36%) one cylinder -114 (57%) two cylinders -14 (7%) three cylinders Diameters ranged from 7 to 32 mm N = 112 group: -41 (37%) one cylinder -63 (56%) two cylinders -8 (7%) three cylinders Diameters: 7-32 mm Lysholm score: used to assess functional outcome / knee function WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) : assesses the development and progression of osteoarthritis		OUTCOMES RELATED TO DONOR SITE -92 very satisfied -70 moderately satisfied -14 neutral -12 moderately unsatisfied -12 very unsatisfied **Lysholm score**: 86 ± 17 points -69 excellent (98-100 points) -35 good-excellent (92-97) -38 fair-good (82-91) -38 fair (66-81) -20 poor (<66) **WOMAC score**: 7.6% ± 0.1% -174 minimal disease (0-19%) -20 mild disease (20-44%) -4 moderate disease (45-69%) -2 severe disease (70-94%) -0 extreme disease (95-100%) N = 112 group: -53 very satisfied -41 moderately satisfied -7 neutral -5 moderately unsatisfied -6 very unsatisfied **Lysholm score**: 89 ± 17 points -51 excellent (98-100 points) -21 good-excellent (92-97) -15 fair-good (82-91) -16 fair (66-81) -9 poor (<66)

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics and treatment	Intervention	Complications/safety outcomes
							WOMAC score: 5.5% ± 0.1% -102 minimal disease (0-19%) -8 mild disease (20-44%) -1 moderate disease (45-69%) -1 severe disease (70-94%) -0 extreme disease (95-100%) -Number of grafts, size of the transplanted cylinders, and patient age did not influence either the Lysholm or the WOMAC score -Higher body mass index and lower general satisfaction ratings negatively influenced the Lysholm and WOMAC scores **Complications:** -3 early infections (diagnosed and treated promptly and healed without additional problems)
Reddy	Case series LoE: IV **Funding:**	F/U: 47 months (range, 7 to 77 months) 73% F/U (11/15)	N = 15 Mean age: 29 years (range, 21 to 44 years) 45% male (5/11) **Symptom duration**: **Previous surgery**: Arthroscopy	**Inclusion**: • Presence of a symptomcatic osteochondral lesion of the weightbaring dome of the talus mearuing approximately 1 cm in length or larger • Failure of nonoperative and arthroscopic treatment **Exclusion**:	Etiology, n patients (%) 100% OCD Trauma, n = 10 Unknown, n = 5 **Localization (n)**: • Medial (10) • Posteromedial (1) • Anterocentral (1) • Central (1) • Lateral (1) • Anterolateral (1) **Mean defect size**: 57.8mm^2 (excellent group)	Mosaicplasty **Intervention**: Diagnostic arthroscopy Margins defined using a Freer elevator Anterolateral portal Debrided with an oscillating arthroscopic shaver Smith and Nephew mosaicplasty set Ankle arthrotomy for osteochondral graft placement	**Failures** NR **Safety Outcomes** Lysholm score No pre-operative Lysholm score. Mean postoperative score: 81 (range 49 to 100) By Lysholm criteria, 5 rated as excellent, 2 as good and 4 as poor. **SF-36** • General health mean score, 50.55 ± 10.18 (range,

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics and treatment	Intervention	Complications/safety outcomes
				• NR	62.1mm^2 (good/poor group, *P*=0.83 when compared to excellent group) **Number of grafts (n)**: 1 (0) 2 (5) 3(7) 4(3) Mean, 2.9 grafts	11 patients who had a medial talar dome lesion underwent a medial malleolar osteotomy for exposure. • All grafts harvest from the ipsilateral knee by arthroscopy or arthrotomy from the intercondylar notch or the lateral femoral condyle proximal to the sulcus terminale. • Grafts were 3.5, 4.5 and 6.5 mm in size. **Cointerventions**: Patients with knee grafts had a similar but more intensive rehab. • Non-weight bearing for 4 weeks • Advanced to cam walker for 6 to 8 weeks. • For rehab of the knee, patients underwent a progressive physical therapy protocol emphasizing strengthening and range of motion.	29.1-63.9; *P*-0.86) (n = 11) • Physical functioning mean score, 47.85 ± 8.16 (range, 31.78-57.03; *P*=0.48) • Mental health mean score, 52.82 ± 10.61 (range, 30.30-64.09; *P* = .35). **AOFAS ankle-hindfoot scale scores (n = 8)** Mean score of 77 (range, 42-100)
Iwasaki	Case series LoE: IV **Funding:**	F/U: months	N = 11 (competitive atheletes) Mean age: 14 years (11-22 years) 100% male • Baseball, n = 8; • Rugby, n = 1; • American football, n = 1; • Soccer, n = 1.	**Inclusion**: • Underwent mosaicplasty between March 1993 and October 2005 for capitellar osteochondrtitis dissecans **Exclusion**:	Etiology, n patients (%) • Capetillar osteochondritis, dissecans, n = 11 (100%) • **Localization (n)**: Elbow joint (11) **Mean defect size (surface area):** 145.4 mm^2 (range	Mosaicplasty **Intervention**: • Subchondral fibrous tissue was curetted • Small (2.7-6.0mm in diamtere, 10-15mm in length) cylindrical grafts were obstained from	**Failures/revisions/reoperations** None **Safety Outcomes** • Lysholm score postoperatively, 99.6 points. • International Knee Documentation Committee Evaluation Form, all normal.

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics and treatment	Intervention	Complications/safety outcomes
			Symptom duration: NR **Previous surgery**: None	• NR	49-270mm^2) **Number of grafts (n)**: • 2 (4) • 3 (2) • 4 (2) • 5 (3)	the lateral periphery of the femoral condyle at the level of the patellofemoral joint. **Cointerventions**: All patients had the same rehabilitation. • A drain was inserted into the joint and removed 24 to 48 horus postoperatively. • Less weight bearing gait at 2 days and allowed to walk freely at days postoperatively. • No other specifically direct rehabilitation of the knee.	MRI score: 6.7 (n = 9)
Nishimura	Case series LoE: IV **Funding:**	Mean F/U:34.4 months (min 24 months)	N = 12 Mean age: 14.4 years (range, 12-17 years) 100% male Baseball, n = 10; Softball, n = 1; Javelin, n = 1 **Symptom duration**: The period between the start of elbow pain and surgery averaged 10.3 months (range, 2-48 months) **Previous surgery**: None	**Inclusion**: • NR **Exclusion**: • NR	Etiology, n patients (%) • Osteochondritis, dissecans athe humeral capitellum, n = 15 (100) **Mean defect size**:NR **Number of grafts (n)**:	**Intervention**: • **Concomitant interventions**: • **Cointerventions**: •	**Safety Outcomes** • Lysholm score: 10 patients with 100 points on the score (max, no pain and full use of joint) • Pain – VAS: Pain free with a score of zero, n =10 • Join effusion: Post-op no patients had joint effusion. • Radiographic findings: No patients had knee osteoarthritis at 12 months post-op. • Muscle strength (60 and 180 deg/sec): reduced muscle strength at 3 months compared with the pre-op level although 11 patients reached pre-op knee extensor muscle

Author (year)	Study design (LoE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, exclusion	Defect/Lesion Characteristics and treatment	Intervention	Complications/safety outcomes
							strength at 12 months.

Table J5: Characteristics of Prognostic studies, Autograft

Author (year)	Study Design (LOE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, Exclusion	Prognostic Factors and Outcomes*	Results†	Summary

Author (year)	Study Design (LOE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, Exclusion	Prognostic Factors and Outcomes*	Results†	Summary
Hangody (2010)	Case series LOE IV Funding: NR	6 weeks, 3 months, 6 months, yearly (% f/u NR) 24 months (88% f/u): mean 9.6 years (2 – 17) 17 years (66%)	N = 354 knee and ankle mosaicplasty transplants Age: mean 24.3 years (14 – 49) Sex: 52% male All patients elite-level athletes	Inclusion: follow-up > 2 years Exclusion: NR	**Knee (n = 303)** Lesion location: medial femoral condyle (187/303, 62%), lateral femoral condyle (74/303, 24%), medial tibial condyle (1/303, 0.3%), lateral tibial condyle (15/303, 5%), patella (18/303, 6%), trochlea (8/303, 3%) Lesion size: 2.5 cm^2 (1.0 – 5.0) No. of plugs: 2.9 (1 – 9) Concurrent procedures: 74% of patients HSS scores: mean preoperative score 67 Arthritis grading (preoperative): Grade 0: 221/303, 73% Grade I-II: 82/303, 27% **Ankle (n = 39)** Hannover score: mean preoperative score 63	**Knee (n = 303)** Clinical scores (% patients reporting excellent/good results): femoral condyle (91%), tibial condyle (86%), patellotrochlear (74%), talar (92%) Adverse events: sepsis (2/303, 0.7%), thromboembolic events (3/303, 1%) Donor site morbidity: 15/303, 5% (with 9/303, 3% in medial femoral) HSS scores (administered to all patients): mean postoperative score 89 Significant improvement from baseline for medial femoral (*P* = .032), lateral femoral (*P* = .024), and lateral tibial (*P* = .015) 2nd look arthroscopy (n = 21): congruent gliding surface recipient site/acceptable coverage donor site (16/21, 76%), degenerative changes at recipient or donor site (5/21, 24%) Progression of Arthritis: For preoperative Grade 0 patients: 194/221, 88% remained Grade 0; 27/221, 12% condition worsened to Grade I-III. For preoperative Grade I-II patients: 57/82, 70% remained Grade I-II; 25/82, 30% condition worsened to Grade II-III. **Ankle (n = 39)** Hannover score: mean postoperative score 91 **Knee and Ankle (n = 354)** Return to sports: 63% (n = NR) (mostly < 30 yrs old) returned to same level of activity; 28% (n = NR) (mostly > 30 yrs old) returned to lower level; 9% did not resume any sports activity	Results on elbow (n = 12) mosaicplasties not presented in report due to limited data. Authors' conclusions: • A combination of 6.5 mm and 8.5 mm grafts might result in better outcomes than that of smaller sizes. • No observation of significant differences in outcome between medial and lateral femoral condyles. • Patellofemoral moscaicplasties experienced lower success rate than femoral condyle surgeries in comparing pre- to post-HSS scores within each treatment group. • Defect size/location, alignment of affected lower extremity, filling rate of defect area, and age of patient are important in long-term outcome; gender is not important. • Increased defect size might correlate with radiological deterioration: larger defects and patellofemoral lesions had poor income vs smaller defects and condylar lesions.

Author (year)	Study Design (LOE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, Exclusion	Prognostic Factors and Outcomes*	Results†	Summary
Haasper (2008)	Retrospective cohort LOE IV Funding:	6 wks, 12 wks, 12 months (% f/u NR) 24 months (12 – 43 months) (% f/u NR)	N = 14 talus mosaicplasty (donor site: condyles of ipsilateral knee joint) Age: mean 24.8 (17.9 – 31.7) Sex: 43% male Indications: OCD Herde grade III/IV (n = 11), posttraumatic osteochondral talus lesions (n = 3)	NR	Lesion location: medial talus (11/14, 79%), lateral talus (3/14, 21%) Lesion size: 6.9 cm^2 (3.7 – 10.1) No. of plugs: 1 (6/14, 43%), 2 (7/14, 50%), 5 (1/14, 7%); mean 1.8 Prior mosaicplasty: previously untreated (8/14, 57%), previously treated (6/14, 43%) VAS ankle scores, preoperative (mean score): previously untreated (6.8 ± 2.5) vs previous treated (7.5 ± 1.9) (ns) Overall VAS score, preoperative: all patients 6.9 ± 2.1; previously untreated (6.8 ± 2.5) vs previously treated (7.5 ± 1.9) (ns)	Return to sports (% patients previously untreated vs previously treated): same sports level (4/8, 50% vs 2/6, 33%), lower level (2/8, 25% vs 2/6, 33%), stopped sports (2/8, 25% vs 2/6, 33%) VAS ankle scores, postoperative (mean score): previously untreated (4.8 ± 1.8) vs previous treated (2.9 ± 2.4) *(P = .218)* Donor knee pain, VAS postoperative (mean score): all patients (2.6 ± 2.4); previously untreated (3.4 ± 1.7) vs previous treated (1.5 ± 2.8) (*P* = .15) Overall VAS score, postoperative (mean): all patients 3.6 ± 2.8; previously untreated (4.1) vs previously treated (2.6) (ns) MRI scan at 12 months: in 10/14, 71% patients: complete incorporation, appropriate congruity of joint surface, and viable transplants. Adverse events: none observed	Author's conclusions • No significant differences among patients with previous mosaicplasty vs patients with no previous mosaicplasty. • Clinical outcomes appear satisfactory in both groups and improved from pre- to post-surgery.

Author (year)	Study Design (LOE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, Exclusion	Prognostic Factors and Outcomes*	Results†	Summary
Marcacci (2005)	Case series LOE IV Funding: NR	24, 36, 48 months (%f/u NR)	N = 37 knee mosaicplasty transplants Age: mean 29.5 years Sex: 73% male All patients professional or amateur athletes	Inclusion: age < 50 years, Outerbridge grade IV of medial or lateral femoral condyle < 2.5 cm^2 Exclusion: lesions > 2.5 cm^2 or < 1.5 cm^2, noncorrected axial deviation, knee stability	Lesion location: medial condyle (23/37, 62%), lateral condyle (14/37, 38%) Lesion size: 2.1 cm^2 (1.8 – 2.5) No. of plugs: 1 (8/37, 22%), 2 (20/37, 54%), 3 (5/37, 14%), 4 (4/37, 11%) Chronicity: acute (12/37, 32%), chronic (25/37, 68%) Concurrent procedures: 23/37, 62% of patients Prior surgeries (% patients): of chronic patients (19/25, 76%) Age group (% patients): young patients (16 – 30 years) (25/37, 68%), older patients (≥ 30 years) (12/37, 32%) ICRS preoperative score (% patients): class C abnormal (23/37, 62%), class D severely abnormal (14/37, 38%)	**% Patients reporting excellent/good results on ICRS score** Lesion location: lateral condyle (14/14, 100%) vs medial condyle (15/23, 65.2%) (*P* = .003) Chronicity: acute (10/12, 83.3%), chronic (19/25, 76%) (ns) Concurrent procedures: concurrent procedure (22/23, 96%) vs no concurrent procedure (7/14, 50%) (*P* = .007) Prior surgeries: prior surgery (14/19, 74%) vs none (15/18, 83%) (ns) Age group: young patients (16 – 30 years) (20/25, 80%) vs older patients (≥ 30 years) (9/12, 75%) (*P* = .02) **% Patients** ICRS score at 24 months (% patients): class A normal (14/37, 38%), class B nearly normal (15/37, 41%), class C (5/37, 14%), class D (3/37, 8%) Brittberg/ICRS defect-repair score: second-look arthroscopy in 5/37 (13.5%) patients: 9-11 points (nearly normal) (3/5, 60%), 5 – 7 point (abnormal) (2/5, 40%) Return to sports: more consistent for lateral condyle vs medial condyle (n, % NR) (*P* = .05) Unable to return to sports: lateral condyle (0/14, 0%) vs medial condyle (5/23, 22%) Adverse events: none observed; no donor site morbidity; failed grafts (3/37, 8%)	Followup not long enough to determine durability or long-term survival of graft. Study comprised of patients with relatively small lesions. Inconsistent reporting of failed cases: report mentions 2 and 3 failed cases. Authors' conclusions: • Mosaicplasty gives reliable results for relatively small lesions with traumatic onset in younger patients. • Patients with lateral condyle lesions had significantly better outcome, however lateral lesions were mostly in younger patients. • Patients with relatively large defects (and therefore larger no. of plugs) had worst clinical outcome. • Smaller defect size and lower no. of plugs statistically significantly correlated to best clinical results (*P* = .049) • A non-significant trend for better results was observed for acute lesions. • Patients who were younger or underwent concurrent procedure had significantly better outcome. • In all 3 failed cases 2 – 3 plugs were used, although arthroscopy was done on only 5 patients.

Author (year)	Study Design (LOE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, Exclusion	Prognostic Factors and Outcomes*	Results†	Summary
Baltzer 2005	Case series LOE IV Funding: NR	3, 6, 9, 12, 24, 36, 48 months, (0 – 4.5 years, %f/u NR)	N = 43 ankle mosaicplasty transplants (donor site: lateral condyle ipsilateral knee joint) Age: mean 31.2 years (range NR) Sex: 70% male	Inclusion: traumatic/nontraumatic osteochondral defects, chondral/osteochondral talus defects Outerbridge III/IV to a maximum of 4 cm^2, age between 14 and 55 years, stable ligaments of ankle, absence of severe knee pain or injury Exclusion: general OA or instability of ankle, deviation in axis of leg, defects > 4 cm^2, OA of knee	Lesion location: medial talus (27/43, 63%), central talus (2/43, 5%), lateral talus (14/43, 33%) Lesion size: 1.7 cm^2 (maximum size 3.7 cm^2) No. of plugs: 1 (15/43, 35%), 2 (20/43, 47%), 3 (8/43, 19%); mean 1.8 Subjective pain, constant/daily pain, preoperative: 41/43, 95% VAS score, mean (preoperative): 4.4 Evanski and Waugh ankle joint score, preoperative: 52 points Mazur ankle joint score, preoperative: 53 points	Subjective pain, constant/daily pain: 1/11, 9% VAS score, mean: 2.3 at 6 months, 1.6 at 12 months, 1.1 at 24 months ROM of defect ankle (months to reach full ROM when compared to contralateral ankle): 1 plug, 8/15, 53% patients with f/u: 24 months 2 plugs, 4/20, 20% patients with f/u: > 24 months 3 plugs, 8/8, 100% patients with any f/u: never reached full ROM Evanski and Waugh ankle joint score, f/u NR: 88 points Mazur ankle joint score, f/u NR: 90 points Adverse effects: none documented Donor site morbidity: 1/43, 2% 2nd look arthroscopy (n = NR), at 6 – 9 months: good cartilage integration	Study experienced significant LTF: 31/43 (72%) patients with f/u at 12 months and 19/43 (44%) patients with f/u at 24 months. Authors' conclusions: • Smaller diameter transplants resulted in better pain reduction and ROM • Best results seen in young sporting adults with post-traumatic defect, treated by anterior approach, and single plug. • Patients receiving 2 plugs achieved nearly full ROM at early f/u but took longer to reach full ROM vs patients receiving 1 plug.

Author (year)	Study Design (LOE) Funding	Study period Follow-up (% followed)	Patient Characteristics	Inclusion, Exclusion	Prognostic Factors and Outcomes*	Results†	Summary
Andres 2003	Retrospective cohort LOE III Funding: NR	≥ 24 months, (24 – 48 months, 100% f/u)	N = 22 consecutive knee OATS (19 patients) Age: mean 55.0 years (44.7 – 65.3) Sex: 32% male Group 1 (n = 8 knees): 1 lesion, OATS treatment Group 2 (n = 7 knees): > 1 lesion, OATS and debridement Group 3 (n = 3 knees): 1 patellofemoral lesion and evidence of poor patellar tracking, OATS and Maquet tibial tubercle elevation treatment Group 4 (n = 4 knees): 1 medial femoral condyle lesion, OATS and closing wedge proximal tibial osteotomy treatment	Inclusion: insidious onset of knee pain, continued symptoms despite ≥ 6 months nonoperative treatment with NSAIDs, joint space narrowing and/or osteophyte formation on preoperative radiographs, documented full-thickness articular cartilage defect in 1 or 2 areas of knee. Exclusion: history of OCD, traumatic osteochondral lesions, inflammatory arthritis, evidence of grade 3 or 4 arthritic changes involving ≥ compartments using Kellgren-Lawrence 4-point scale	Lesion size: 2.4 ± 0.9 cm^2 No. of plugs (% patients): mean 2.8 ± 1.1	WOMAC Index: group 1 significantly better score (14.9 ± 6.9) than group 2 (51.7 ± 26.2) (*P* = .002); group 3 (38.7 ± 17.9), group 4 (58.0 ± 13.3) VAS score: group 1 significantly better score (3.8 ± 1.2) than group 2 (6.6 ± 2.3) (*P* = .025); group 3 (7.0 ± 2.0), group 4 (6.1 ± 1.7) SF-36: no significant difference between groups in any category Subjective assessment, overall status of knee rated improved compared to preoperative (% knees): group 1 (7/8, 88%), group 2 (3/7, 43%), group 3 (1/3, 33%), group 4 (1/4, 25%) (ns) Arthritis scoring on radiograph at 24 months (19/22 knees evaluated): 17/19 knees (89%) no changes compared to preoperative Adverse effects: overall 5/22 knees (23%); reflex sympathetic dystrophy (group 2: 1/7, 14%), subsequent total knee replacement (group 2: 1/7, 14%), lysis of adhesions/manipulation (group 3: 1/3, 33%; group 4:1/4, 25%), displacement of proximal tibial osteotomy (group 4: 1/4, 25%)	Authors' conclusions: • Good results when OATS used to treat solitary defect. • Poor results when OATS or OATS and concurrent procedure used to treat multi-focal defects. • Recommends not using OATS when treating multiple osteochondral lesions or multicompartmental arthritis. • Study limitations include short-term follow-up, no preoperative measures were recorded, baseline differences among four treatment groups

NR: not reported; f/u: follow-up; LTF: loss to follow-up; LOE: Level of Evidence; ns: not statistically significant; OCD: osteochondrosis dissecans; OA: osteoarthritis; ROM: range of motion; NSAIDs: nonsteroidal anti-inflammatory drugs
Note: percentages might not add to 100% due to rounding.
*Hannover questionnaire for foot and ankle rates patient's complaints and the functional status based on a severity-symptom scale and functional status (maximum 100 points, higher scores indicate higher level of function); HSS (Hospital for Special Surgery) score, clinician-based outcome (scale 0 – 100 points, lower score indicates greater disability) [Hangody, 2010]. VAS (Visual Analogue Scale): measures pain intensity (scale 0 – 10, highest score indicates worst imaginable pain) [Haasper, 2007; Baltzer, 2005]. Evanski and Waugh score (scale NR); Mazur ankle clinician-based outcome (scale 0 – 100 points, lower score indicates poorer outcome) [Baltzer, 2005]. Chronicity: acute indicates that patients had a traumatic chondral lesion at least 3 weeks before surgery; concurrent procedures indicates other procedures (e.g., ACL reconstruction, meniscectomy, ligament repair) performed during the mosaicplasty [Marcacci, 2005].

† Clinical scores include the HSS, Lysholm, Cincinnati, and ICRS scores; arthritis grading based on Fairbanks scale [Hangody 2010]. Good/excellent ICRS score (maximum score 100, higher scores indicate higher level of function and lower level of symptoms) not defined; Brittberg/ICRS defect-repair score based on arthroscopy (maximum score 12 points, higher scores indicate better cartilage repair) [Marcacci, 2005]. WOMAC (Western Ontario and McMaster Universities Osteoarthritis index) (scale 0 – 100, 100 indicating worst pain, stiffness, and function); VAS (Visual Analogue Scale) measures pain intensity (scale 0 – 10, highest score indicates worst imaginable pain); SF-36 (Short Form-36) assesses healthcare-related quality of life (scale 0 – 100, higher score indicates positive health status); arthritis scoring using Kellgren and Lawrence scoring, 4-point scale; instrument for overall subjective knee assessment not specified [Andres, 2003].

Appendix K. Peer Reviewers

The individuals listed below have agreed to provide clinical and/or peer review.

This role should not be construed to mean that the individuals were authors or contributors to the formulation of the draft, nor does it imply endorsement, approval, or disapproval of the process or report.

Individual	Relevant Expertise/Experience
Michael Buschman, PhD Professor, Department of Chemical Engineering and Institute of Biomedical Engineering Ecole Polytechnique of Montreal Affiliated Researcher, Department of Pathology and Cell Biology, Faculty of Medicine, University of Montreal	▪ PhD, Massachusetts Institute of Technology, Medical Engineering and, Medical Physics; Thesis Title: Chondrocytes in Agarose Culture: Development of a Mechanically Functional Matrix, Biosynthetic Response to Compression and Molecular Model of the Modulus ▪ Over 25 years research experience and mentorship of graduate students related to basic science of cartilage function, damage and repair with numerous publications and three patents ▪ Memberships (selected): Orthopedic Research Society, International Society for Cartilage Repair; Board Member International Cartilage Repair Society ICRS ▪ Editorial Boards (selected): Cartilage, Osteoarthritis and Cartilage, ▪ Editor/organizer of 2010 Special Issue containing ICRS recommendations on the conduct of cartilage repair studies
Christopher J. Wahl, MD Associate Professor, Team Physician University of Washington Department of Orthopaedics and Sports Medicine Director of Arthroscopic Education	▪ M.D., Yale University School of Medicine, New Haven, Connecticut, (ΑΩΑ), 1996 ▪ Board certified, American Board of Orthopaedic Surgery ▪ Over 15 years of funded clinical research in orthopedics ▪ Peer reviewer: *Arthroscopy, The Journal of Arthroscopic and Related Surgery, The American Journal of Sports Medicine (AJSM), The Journal of Shoulder and Elbow Surgery (JSES), The Journal of the American Academy of Orthopaedic Surgeons (JAAOS)* [Knee, Shoulder, Sports Medicine, Cartilage Reconstruction] ▪ Memberships (selected): Alpha Omega Alpha (ΑΩΑ), American Orthopaedic Society for Sports Medicine (AOSSM), Fellow, American Academy of Orthopaedic Surgeons (AAOS), American College of Sports Medicine (ACSM), Magellan Society (AOSSM)