

## Evidence Summary AMIC® Chondro-Gide®



## Contents

What's in it for You?



From levels of evidence to levels of confidence.

## Follow-Up

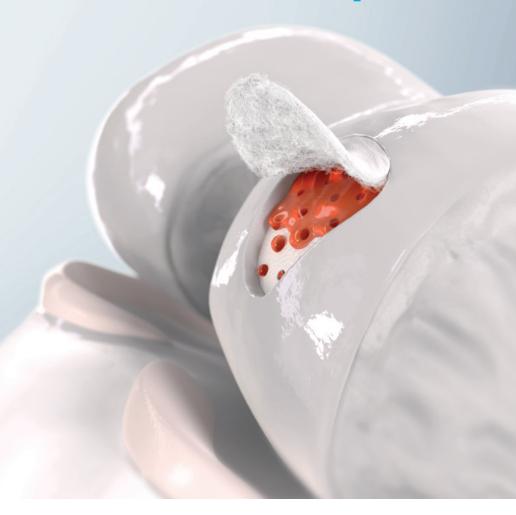
#### 10 Years and Counting

AMIC® Chondro-Gide® was developed to support regenerative approaches in cartilage treatment. It is a procedure that meets the requirements of surgeons and patients alike:

- Minimally invasive one-step procedure1
- Positive long-term outcome<sup>2,3,4,5,6,7,8</sup>
- Cost-efficient<sup>6,9</sup>

The collected data for the treatment of cartilage defects in the knee, ankle and hip have demonstrated that AMIC® Chondro-Gide® provides stable results for up to 10 years after surgery.<sup>2,3,7,8</sup> Patients regain joint function and more invasive procedures can be postponed or avoided altogether.

## 1-step procedure wins **15 000 000** steps<sup>10</sup>



#### 20 Years AMIC®

AMIC® Chondro-Gide® was developed in collaboration with leading surgeons in Europe to stimulate and support the body's potential to heal itself. Because the self-healing ability of the avascular and aneural articular cartilage is limited, AMIC® recruits cells from bone marrow to the defect.

Bone marrow stimulation (BMS) induces the cascade of events needed to form new tissue. The Chondro-Gide® collagen membrane is used to cover the defect to keep cells in place and protect the newly formed tissue from shear forces in the joint. The techniques for BMS may vary, but clinical data indicates that the defect

preparation should include the removal of the calcified layer until petechial bleeding occurs. 11, 12, 13 This step may be enough to jumpstart the regenerative cascade.

Such minimally invasive treatments, which reduce stress to the subchondral bone, are currently being tested.

- Schagemann et al. 2018, Arch Orthop Trauma Surg 138 (Clinical study)

- Raiser et al. 2020, Arch Orthop Trauma Surg 135 (Clinical Study)
  De Girolamo et al. 2019, J Clin Med 8(3) (Clinical Study)
  Walther et al. 2020, Foot Ankle Surg 27(3) (Meta-analysis)
  Walther et al. 2014, Oper Orthop Traumatol 26 (Clinical Study)
- Benthien & Behrens 2010, Knee Surg Sports Traumatol Arthrosc 19(8)
- Gille et al. 2023, BMC Musculoskeletal Disorders 24(1) (Clinical study)
- Volz et al. 2024, Eur J Orthop Surg Traumatol, 28(4) (Clinical study)

- 9 Fossum et al. 2019, Orthop J Sports Med 7(9)(Clinical study)
  10 Althoff et al 2017, Nature 547 (Data analysis)
  11 Steadman et al. 1997, Oper Techniques in Orthop 7 (Clinical study)
- 12 Frisbie et al. 2006, Am J Sports Med 34(11)(Pre-clinical study)
- 13 Steadman et al. 2010, Cartilage 1(2) (Clinical study)

## >140 Peer-Reviewed **AMIC® Publications\***

#### We Invest in Evidence to Win Your Confidence

The use and clinical results of the Chondro-Gide® membrane for the treatment of cartilage lesions in the knee, ankle, hip and MTP joints have been studied in more than 4,000 patients by numerous research teams around the world.

AMIC® and Chondro-Gide® have been included in national and international consensus recommendations. 1,2,3,4





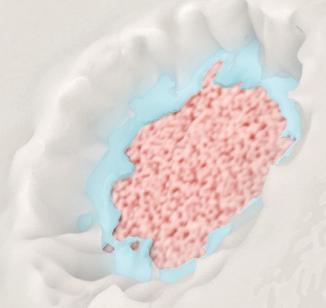
AMIC® in the hip joint



AMIC® in the MTP joint



AMIC® in the knee joint



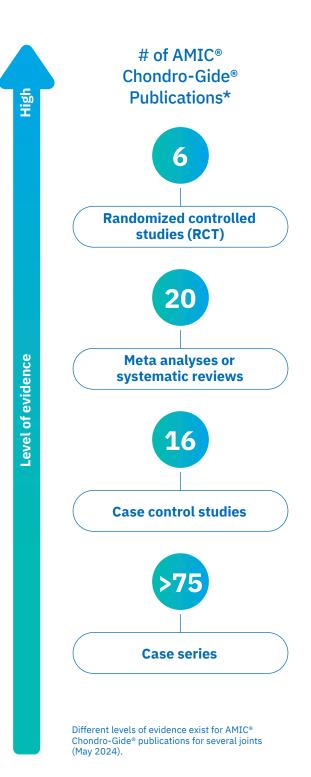
- Niemeyer et al. 2023, Z Orthop Unfall 161(1) (Guidelines) Walther et al. 2024, EFORT Open Reviews 9(3)(Guidelines) Fickert et al. 2017, Z Orthop Unfall 155(6)(Guidelines) Rothrauff et al. 2018, Foot Ankle Int 39

- (Consensus meeting)

<sup>\*</sup> You can download the Reference List Chondro-Gide® from the downloads section on www.geistlich-ortho.com



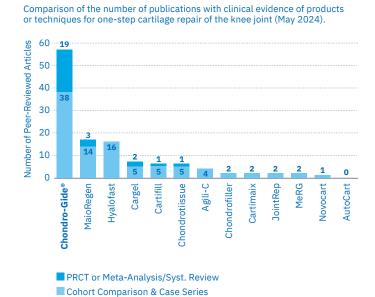
## Levels of Evidence



In 2018, the German Orthopaedic and Trauma Society (DGOU) Working Group on Tissue Regeneration released their consensus statement for knee cartilage treatment with matrix-augmented bone marrow stimulation. They compared 11 products and concluded that there was considerable variation in the quality of the studies about them.¹ Chondro-Gide® had the highest number of peer-reviewed publications and also higher level of evidence such as randomized control trials.

Since 2018, a significant number of new peer-reviewed papers on Chondro-Gide® were published in international journals, among them two meta-analyses on AMIC® in the knee joint and ankle joint.

In 2023, the DGOU published an update of the consensus statement, with input from more than 30 cartilage experts. The updated recommendations include matrix-augmented bone marrow stimulation (m-BMS) as a standard method for the treatment of cartilage defects with a size of 1–4,5 cm<sup>2</sup> and osteochondral defects with a size of 0–4 cm<sup>2</sup>. Chondro-Gide® was highlighted again as the biomaterial with the best evidence within the m-BMS group.<sup>2</sup>



<sup>1</sup> Niemeyer et al. 2018, Z Orthop Unfall 156(5)(Guidelines)

<sup>2</sup> Niemeyer et al. 2023, Z Orthop Unfall 161(1) (Guidelines)

## META Analysis means MEGA Confidence



#### AMIC® in the Knee Joint

The first meta-analysis of a one-step cartilage repair procedure in the knee using the Chondro-Gide® membrane demonstrated significant and clinically meaningful improvement in pain (VAS 4.8 points) and functional scores (Lysholm and IKDC) compared to preoperative values over a follow-up period of more than 3 years.¹

The meta-analysis identified 66 publications through systematic searches performed in the PubMed and Embase databases as well as in other sources using the search terms: "Chondro-Gide®", "AMIC®", "cartilage", and "knee". The following inclusion criteria were applied: clinical study

with a minimum of 6 patients, cartilage defects in the knee, and primary measures of pain and function.

#### 12 publications met the criteria.

These studies included 375 patients, mean age: 36.2 years (range, 14–70 years), with chondral and osteochondral defects Outerbridge Grade III & IV with a minimum follow-up of 2 years.

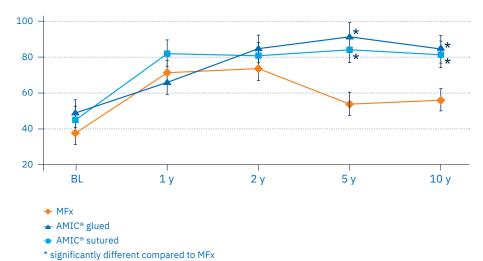
The improvement was maintained for more than 5 years which confirms the mid-term success of AMIC® Chondro-Gide® in the treatment of Outerbridge grade III & IV lesions with an average size of 4.2 cm².

Less than 1% (3/375) of the cases required conversion to arthroplasty.

The good results for AMIC® Chondro-Gide® were recently confirmed in a randomized controlled trial (RCT). 47 Patients received either an arthroscopic microfracturing (MFx) or an AMIC®. The AMIC® patients were further split into two subgroups where the Chondro-Gide® was either sutured or glued.

No treatment related serious adverse event for any patient has been observed. AMIC® patients had significantly better outcomes than those treated with MFx and improvement was maintained from 2 to 10 years after surgery.<sup>2</sup>

The modified Cincinnati score improved in all 3 groups for the first 2 years. While in the AMIC® groups the improvement was maintained from 2 to 10 years, the MFx group deteriorated significantly.²



<sup>1</sup> Steinwachs et al. 2019, Cartilage 13(1)(Meta-analysis)

<sup>2</sup> Volz et al. 2024, Europ J Orthop Surg Traumatol 28(4) (Clinical study)



#### AMIC® in the Ankle Joint

The first meta-analysis of pain and functional outcomes following AMIC® Chondro-Gide® treatment of osteochondral lesions of the talus (OLT) demonstrated significant improvement compared to the baseline.

The meta-analysis compared the pain VAS, the American Orthopedic Foot and Ankle Score (AOFAS), and the Foot Function Index (FFI) between baseline and follow-up of 1–2 and 3–5 years.<sup>1</sup>

48 publications were identified in systematic searches in PubMed and Embase databases. Studies were included (PRISMA guidelines) if they had primary measures of clinical outcomes, a minimum of 1-year follow-up, and included more than 5 patients.

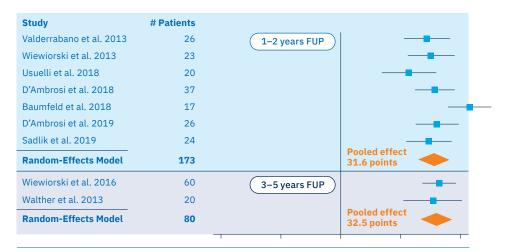
- Qualitative analysis: 15 studies /
   492 patients
- Quantitative analysis: 12 studies / 323 patients
- Mean age: 36 years (range, 12-68)
- OCL size 1-2.4 cm²
- Different surgical approaches and bone marrow stimulation (BMS) techniques
- Mean follow-up: 33 months (range, 12–60)

The AMIC® Chondro-Gide® procedure for treatment of OCL of the talus provided clinically relevant and significant improvement in ankle joint pain and in functional outcome scores (AOFAS, FFI) up to 5 years after surgery.

None of the patients required conversion to ankle fusion or arthroplasty.

Numerous recent publications on the treatment algorithms for OLT have led to an update of the DGOU guidelines for the operative management of OLT. M-BMS techniques such as AMIC® are recommended to stabilize the bone graft in cystic OLT and in lesions larger than 1 cm². Within the group of m-BMS, Chondro-Gide® has the best clinical evidence supporting its role as an essential element in the treatment of OLT.²

Improvement in AOFAS compared to baseline.



<sup>1</sup> Walther et al. 2020 , Foot Ankle Surg 27(3) (Meta-analysis)

<sup>2</sup> Walther et al. 2024, EFORT Open Reviews 9(3) (Guidelines)



#### AMIC® in the Hip Joint

The use of AMIC® Chondro-Gide® for the treatment of focal, acetabular chondral lesions associated with femoroacetabular impingement (FAI) is well established. Two systematic reviews and/or meta-analyses and several publications report medium to long-term clinical results after AMIC®.1, 2, 3, 4, 5

In the most recent systematic review and meta-analysis, Lu et al. (2023) assessed the outcomes of hip arthroscopy in patients with FAI syndrome and associated chondral lesions. The review followed the PRISMA guidelines and included 24 studies (3233 hips) that used hip arthroscopy for the treatment of FAI and chondral lesions classified according to the Outerbridge system. The mean age of the patients was 38.4 years. Most studies used MFx to treat grade III and

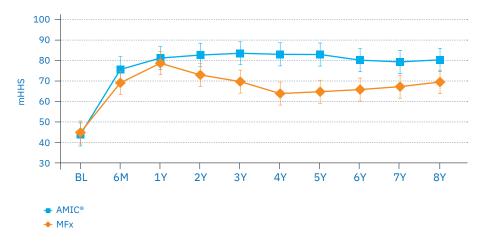
IV lesions, and three studies compared MFx with AMIC® or AMIC®+. Universal improvements in PROMs were reported after hip arthroscopy in patients with FAI-related chondral lesions. However, patients with Outerbridge grade III and IV lesions experienced significantly less improvement. After matching for Outerbridge grade, patients who underwent MFx for cartilage damage had a significantly higher rate of conversion to total hip arthroplasty (THA) and a significantly higher rate of revision arthroscopy compared to patients who underwent AMIC®, suggesting a potential benefit of AMIC® for the treatment of high-grade chondral lesions.1

De Girolamo et al. (2018) compared arthroscopic AMIC® with MFx in patients with chondral defects associated with FAI at 8-year follow-up. Both techniques resulted in a significant clinical improvement in the first year, as measured by the modified Harris Hip Score (mHHS), even in lesions >4 cm<sup>2</sup>. 22% of MFx patients required THA, while none of the AMIC® patients were converted to THA, suggesting stable outcomes after AMIC® over time regardless of lesion size.3

Mancini & Fontana (2014) compared the clinical outcomes of the two-stage arthroscopic matrix-induced autologous chondrocyte implantation (MACI) and the single-stage AMIC® for the treatment of acetabular chondral defects between 2-4 cm<sup>2</sup>. In both the MACI and the AMIC® groups, significant improvements in mHHS were seen from baseline to 3 years postoperatively and remained stable up to 5 years. No significant differences were observed between the groups, suggesting that both procedures are valid for the repair of medium-sized acetabular, chondral defects associated with FAI. However, the single-stage AMIC® was preferred because it offers the same benefits as the two-stage MACI procedure.5

Similar results were reported in young, active patients with mid-sized chondral lesions of the acetabulum. At 2 years after arthroscopic AMIC® treatment, clinical outcome scores showed significant improvement compared to preoperative scores, and these young patients were able to resume sports-related activities after surgery.6

AMIC® results remain stable up to 8 years, while MFx results worsen after 2 years.



Lu et al. 2023, Bone Joint J 105(7) (Systematic review)

Hotham & Malviya 2018, Bone Joint Res 7(5) (Systematic review)

De Girolamo et al. 2018, Arthroscopy 34(11) (Clinical study)

Fontana & de Girolamo 2015, Bone Joint J 97(5) (Clinical study)

Mancini & Fontana 2014, Int Orthop 38(10) (Clinical study)

Thorey et al. 2020, Knee Surg Sports Traumatol Arthrosc 28(7) (Clinical study)



#### AMIC® in the MTP1 Joint

Chondral lesions of the first metatarsophalangeal joint (MTP1) are a common pathological condition of the foot. Left untreated, they can progress to hallux rigidus causing pain and functional impairment.

There are controversial opinions about the optimal treatment of chondral defects in the MTP1 joint. Some support the joint preserving (distraction, cartilage regenerative techniques, OATS, osteotomies) and others the joint sacrificing (arthrodesis, arthroplasty) techniques.

In a large, prospective, consecutive, non-controlled case series, 198 patients with chondral lesions of the MTP1 joint who were treated with AMIC® plus peripheral blood concentrate (PBC) were studied. Most patients also had a deformity that was treated concomitantly. The authors compared the 5-year results with their previously reported 2-year results.¹

The table below shows the number of patients (N) available for 2- and 5-year follow-up with their pain and EFAS scores

at the two follow-up time points. The scores improved markedly compared to preoperative values, but there was no difference between the 2-year and 5-year results.

The authors concluded, that AMIC®+ Peripheral Blood Concentrate as a treatment for chondral defects at MTP1 as part of a joint-preserving surgery resulted in improved and high validated midterm outcome scores.

	Preoperative	2-year FUP	5-year FUP
N	198 (with 238 chondral defects)	176	164
VAS FA (average, range)	46.8 (8.7–79.8)	74.1 (19.1–100)	75.0 (20.3–100)
EFAS Score (average, range)	11.9 (2–22)	17.1 (11–24)	17.3 (11–24)

<sup>1</sup> Richter et al. 2022, Foot Ankle Surg 28(8) (Clinical study)

## We've Got You Covered

The Collagen Membrane: Chondro-Gide®

#### It's BI & BIO

#### **BI** is for **BILAYER**

Chondro-Gide® is a porcine bilayer collagen I/III membrane. It has a unique structure, being compact and smooth on one side and rough and porous on the other.¹

#### **BIO is for BIOCOMPATIBLE**

The collagen bilayer is compatible with the tissues found in the defect.<sup>1</sup>

#### **BIO is for BIOFUNCTIONAL**

The rough, porous layer faces the defect. Cells that are released through BMS techniques attach themselves to this layer, where they proliferate and support the growth of new tissue.<sup>1</sup> The compact top layer protects the cells and newly forming tissue from dislocation and shear forces in the joint. It functions as the roof of a biological chamber that forms over the defect. Overall, the 3D structure and material of the membrane provide a biofunctional environment that fosters cell growth and differentiation. 1,12

#### **BIO is also for BIODEGRADABLE**

The collagen membrane is naturally resorbed without any negative side effects and is slowly replaced by the newly forming tissue  $^{1}$ 



- 1 Geistlich Pharma AG data on file
- 2 Gille et al. 2010, Cartilage 1(1) (Pre-clinical study)

Chondro-Gide® is not approved for sale and usage in all countries or regions by the relevant authorities. Indications of use may also vary by country and region. Please contact your country representative of Geistlich Pharma AG for product availability and information.

#### Chondro-Gide® is Versatile

You can cut, wrap, pull, stretch and suture the membrane.1

#### Carrier

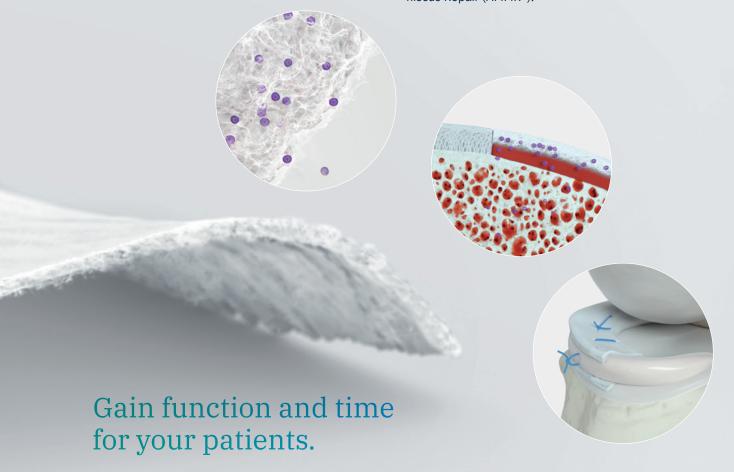
Initially designed as a carrier for autologous chondrocyte implantation (ACI), Chondro-Gide® is an established product for cartilage therapies with >25 years of proven clinical use.2

A recent tissue engineering study including Chondro-Gide® is ENCANTO, a Horizon Europe project that uses nasal chondrocytes cultured on Chondro-Gide® for cartilage regeneration.3,4

#### Cover

Chondro-Gide® has been successfully used for over 20 years in AMIC® to cover cartilage defects. 5,6 Recent studies explore new approaches where AMIC® is augmented with additional cells (e.g. minced cartilage, adipose cells, PRP, BMAC) or bioactive components to enhance the regenerative process.<sup>7,8,9,10,11</sup>

The intended use of Chondro-Gide ® has been extended to augment meniscal repair by wrapping the membrane around the sutured meniscus. 12, 13, 14, 15 The corresponding meniscus wrapping technique is registered as Arthroscopic Matrix-based Meniscus Repair (AMMR®).



- Geistlich Pharma AG data on file (Bench test)
- Steinwachs & Kreuz 2007, Arthroscopy 23(4) (Clinical study)
- Mumme et al. 2016, Lancet 388(10055) (Clinical study) ENCANTO researching a new regenerative therapy https://encanto.health/encanto/
- Steinwachs et al. 2019, Cartilage 13(1)(Meta-analysis)
- Walther et al. 2020, Foot Ankle Surg 27(3) (Meta-analysis) De Girolamo et al. 2019, J Clin Med 8(3) (Clinical study)
- Runer et al. 2023, Knee Surg Sports Traumatol Arthrosc 31(11) (Clinical study)
- Gobbi et al. 2014, Am J Sports Med 42(3)(Clinical study)

- 10 Richter et al. 2022, Foot Ankle Surg 28(8) (Clinical study) 11 Sciaretta et al. 2023, Int Orthop 48(1) (Clinical study) 12 Piontek et al 2012, Pol Orthop Traumatol 77 (Clinical study)
- 13 Piontek et al. 2016, Cartilage 7(2) (Clinical study)
  14 Ciemniewska-Gorzela et al. 2020, Cartilage 13(1) (Clinical study)
- 15 Bakowski et al. 2023, Int Orthop 47 (Clinical study)

## A Versatile Method

## Mini-Open or Arthroscopic? AMIC® Works

The arthroscopic technique is equally positive as the mini-arthrotomy with AMIC® Chondro-Gide®.

A retrospective study compared the clinical outcomes of patients who underwent AMIC® Chondro-Gide® procedures via arthroscopic or mini-open surgery. The study followed patients for up to two years.¹

Both surgical approaches yielded equally positive resultspain and functional scores (Lysholm and KOOS).<sup>1</sup>

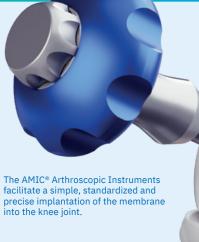
The conclusion that both approachesyield comparable results, has been confirmed by a recent meta-analysis and systematic review. The choice of approach for cartilage repair should consider the surgeon's expertise, location of lesion, and patient-specific factors.<sup>2</sup>

The AMIC® Arthroscopic Instruments were developed to standardize the arthroscopic approach.

The instruments were launched in 2021 and are currently available in selected markets. In both mini-open and arthroscopic techniques, the unique advantage of AMIC® Chondro-Gide® is that it suports the body's potential to heal itself.

### Your choice - AMIC® works

- Knee
- Ankle
- Hip
- Metatarsophalangeal joint
- Glue or suture
- Mini-open or arthroscopic
- Arthroscopic with or without AMIC® Arthroscopic Instruments
- AMIC® or AMIC®+
- Bone marrow stimulation using MFx, drilling, or removal of the calcified layer





2 Tan et al. 2024, J ISAKOS 9(2) (Meta-analysis)



# AMIC® Glued or Sutured? Your Choice

#### Does the Fixation Method Matter?

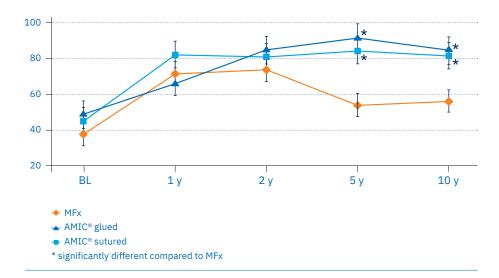
A randomized controlled trial with three arms was conducted to assess the outcomes of AMIC® compared to MFx alone over a 10-year follow-up period. In addition, the efficacy of fixation techniques using glue or sutures was evaluated for AMIC®.

All three treatment groups showed significant improvement after surgery in the first year, followed by stabilization at 2 years, regardless of whether the membrane was glued or sutured.

At 5 and at 10 years, however, the results of the AMIC® Chondro-Gide® patients were significantly better than those of patients treated with MFx alone, regardless of the type of fixation.¹

The type of fixation does not appear to impact the clinical outcome. Therefore, the choice of whether to use sutures or a fibrin-based fixation remains at the discretion of the surgeon.

The modified Cincinnati score improved in all 3 groups for the first 2 years. While in the AMIC® groups the improvement was maintained from 2 to 10 years, the MFx group deteriorated significantly.



<sup>1</sup> Volz et al. 2024, Europ J Orthop Surg Traumatol 28(4) (Clinical study)

## AMIC® vs ACI

#### Is the Two-Step ACI Superior to the One-Step AMIC®?

Chondro-Gide® was initially developed for Autologous Chondrocyte Implantation (ACI) and subsequently became the basis for the one-step treatment approach with AMIC®. The membrane continues to be used successfully in both approaches. However, given the regulatory hurdles and the need for cost-effective cartilage treatments, AMIC® has been described as the more efficient and economical choice compared to ACI.1

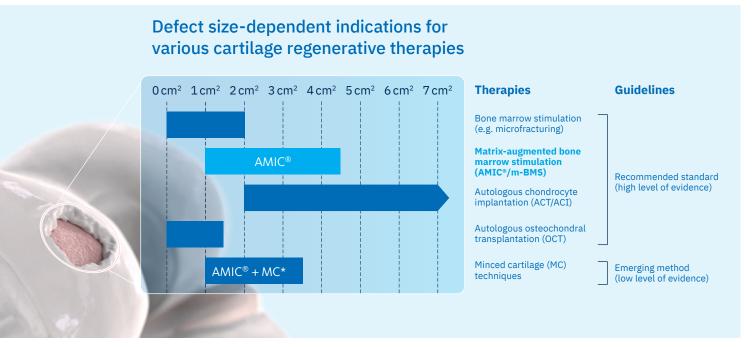
Fossum et al. (2019) compared the outcomes of ACI covered with Chondro-Gide® (ACI-C) and AMIC® for the treatment of chondral or osteochondral defects in the knee. Clinical outcomes at 2 years showed no significant superiority of either ACI-C or AMIC®.

Both cartilage repair methods resulted in significant improvement of average KOOS and Lysholm scores as well as in a significant reduction in pain VAS at 1- and 2-year follow-up, when compared to baseline values.

A very strong statement was made in a systematic review, stating that "AMIC may provide better outcomes than mACI for chondral defects of the knee".2

In another randomized controlled trial from the UK, 390 patients with a failed primary treatment for chondral or osteochondral defects were randomly assigned to receive either ACI or an alternative management, where AMIC® was one option. Subgroup analysis showed comparable results for AMIC® and ACI.3

In the recommendations of the DGOU, there is an overlap of AMIC® and ACI as recommended treatment for focal full thickness cartilage defects with a size between 2 and 4.5 cm<sup>2</sup>.4 Given that AMIC® leads to comparable clinical outcomes as ACI, one should consider several factors in the treatment algorithm. These can be economic factors, but also patient-specific requirements and the fact that AMIC® is a one-stage procedure vs ACI being a twostage procedure.



A symptomatic, full-thickness, focal cartilage defect in the absence of osteoarthritis represents the classic indication for cartilage regenerative therapy.

- \* The majority of published cases were covered with the Chondro-Gide® membrane. 5,6
- Fossum et al. 2019, Orthop J Sports Med 7(9) (Clinical study)
- Migliorini et al. 2022, Br Med Bull 141(1) (Systematic review)
- Snow et al. 2023, Am J Sports Med 51(2) (Clinical study) Niemeyer et al 2023, Z Orthop Unfall 161(1) (Guidelines)
- Massen et al. 2019, Orthop J Sports Med 7(6) (Clinical study)
- Runer et al. 2023, Knee Surg Sports Traumatol Arthrosc 31(11) (Clinical study)

## AMIC®+

#### Combines Current Trends of Biologic Augmentation in Cartilage Regeneration With AMIC® Therapy

The benefit of AMIC®, an established, successful cartilage repair technique is that it provides the foundation for attempting variation and inspiring new developments.

AMIC® is a biological procedure that combines bone marrow stimulation (BMS) with Chondro-Gide®, a unique collagen membrane. Approaches labeled as AMIC®+ combine BMS with additional biological components and Chondro-Gide®. The addition of the biological materials in AMIC®+ is subject to regulations, which vary from country to country. Further research and long-term results are needed to assess the clinical benefit beyond that produced in the

proven AMIC®. Geistlich continuously supports collaborations with regeneration experts and the exploration of new approaches in cartilage repair ther-

# **Minced Cartilage** Fragments9 Platelet-Rich Plasma<sup>6,7,8</sup> **Autologous** Microfragmented Adipose Tissue<sup>5</sup> **Bone Marrow Aspirate** Concentrate<sup>1,2,3,4,7</sup>

- Gobbi et al. 2014, Am J Sports Med 42(3) (Clinical study) De Girolamo et al. 2019, J Clin Med 8(3) (Clinical study)

- Richter et al. 2020, Foot Ankle Surg 26(6) (Clinical study) Steinwachs et al. 2014, Arthrosc Tech 3(2) (Technique paper) Sciaretta et al. 2023, Int Orthop 48(1) (Clinical study)
- Dhollander et al. 2011, Knee Surg Sports Traumatol Arthrosc 19(4) (Clinical study) Hede et al. 2019, Cartilage 13(1) (Clinical study)

- Richter et al. 2022, Foot Ankle Surg 28(8) (Clinical study) Runer et al. 2023, Knee Surg Sports Traumatol Arthrosc 31(11) (Clinical study)

## AMIC® Chondro-Gide®: The one-step cartilage therapy with the best evidence1,2





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Niemeyer et al. 2022: Recommendation of the Working Group Tissue Regeneration of the German Orthopedic and Trauma Society (DGOU) for Treatment of Focal Cartilage Defects of the Knee Joint

<sup>2</sup> Walther et al. 2024: Operative management of osteochondral lesions of the talus: 2024 recommendations of the working group 'clinical tissue regeneration' of the German Society of Orthopedics and Traumatology (DGOU)