4 Pirkimo dalis
Besirezorbuojanti dvisluoksne membrana

Geistlich

Patient Information Leaflet

Chondro-Gide®

Name of material/device and available sizes

Chondro-Gide®
√ 20 x 30 mm 4.5.
30 x 40 mm
40 x 50 mm

4.1. su specialiu folijos šablonu.

The product illustration is exemplary for the product family

Intent and indications for using this material/device

Chondro-Gide® is a resorbable material that is surgically implanted to cover chondral or osteochondral defects treated with marrow stimulation techniques (e.g., AMIC® - autologous matrix induced chondrogenesis). The defects can be acute or chronic and be caused by a fall, accident or other traumatic events. The material gradually resorbs over several months (1 – 4 months) and is replaced by the patient's own tissues. Provided active infection is not present at the surgical site, this material can be safely used in most patients. However, there is no data available on use of this material during pregnancy and lactation, and in children. Until such time that additional data becomes available, it is recommended that Chondro-Gide® be avoided in pregnant and lactating women, and in children.

Patient-specific operating instructions

As Chondro-Gide® is an implantable material that degrades and disappears naturally over time (1 - 4 months), there are no patient-specific operating instructions or maintenance procedures required for this material. It is important that all post-operative instructions and precautions advised by the surgeon are followed and that any post-operative follow-up appointments are attended. This will help reduce the risk of any post-operative complications and maximise the likelihood of a successful clinical outcome. Please contact your surgeon immediately for advice if any signs of post-operative infection (i.e., increase in redness, excessive swelling, worsening pain, fever, malaise, etc.) or allergic reaction (i.e., wheezing, chest tightness, shortness of breath and a cough, and swollen lips/tongue/eyes/face) become evident. Please call an ambulance or attend the nearest hospital Emergency Department in the event of a life-threatening emergency.

How does Chondro-Gide® work?

Chondro-Gide® is a natural collagen material derived from veterinary-certified porcine (pig) tissue. It is carefully purified such that it becomes biocompatible with human tissues. No chemical additives or further cross-linking have been employed, and no residual components are present that can pose a threat to the patient.

The material has two distinct surfaces (i.e., bilayer); a) a smooth (dense) surface which is placed facing the joint space, and b) a rough (porous) surface which is placed against the cartilage

defect. Chondro-Gide® acts to stabilise the chondral tissue repair defects. The smooth (dense) layer facilitates a temporary barrier function; preventing the transplanted chondrocytes or stem-cell enriched blood coagulates from being flushed out of the cartilage defect. The rough (porous) layer supports ingrowth of cells and newly-formed tissues. Chondro-Gide® is hydrophilic and has a fibrous microstructure. When applied, the collagen fibres swell, resulting in an optimal fit onto the cartilage defect. The structural integrity is assured even when wet. Chondro-Gide® can be secured into place by fibrin glue or sutures. The degradation rate and lifetime of the material can be affected by a number of factors including features of the surgical site, blood flow to the site, and patient comorbidities. The material is sterilised by gamma sterilisation.

Potential side effects that can occur

Chondro-Gide® has been proven to be a safe and reliable material. It is derived from natural collagen that is carefully purified to minimise risk of immunological reactions. Nevertheless, any history of collagen or atypical allergies and/or inflammatory joint disease should be discussed with your surgeon prior to using this material (i.e., mammalian meat allergy). As with any surgical procedure, possible side effects that may occur includes swelling at the surgical site, flap sloughing, bleeding, local inflammation/tissue death, and infection. These side effects could lead to reduced tissue healing. Other surgery related disturbances that may appear include bone loss and pain. Increased pain and swelling after surgery for longer periods than expected may be indicative of malfunctioning or failure of the material. If such circumstances arise, immediately contact your surgeon for advice.

Chondro-Gide® is designed and processed in a way that ensures patient safety and avoids compromising the clinical condition of the patient. Although every effort is taken to minimise risks associated with the clinical use of this material, any potential risks and complications that could occur are addressed in this patient information leaflet.

Potential interaction(s) of Chondro-Gide® with other equipment and recommended precautions

Chondro-Gide® is a non-metallic material. It does not demonstrate magnetic behaviour or generate heat during magnetic resonance (MR) examination. Chondro-Gide® has not been specifically studied in the MR environment. In some circumstances, metal hardware may have been employed to secure Chondro-Gide® in position. Please consult with the radiologist/radiographer if this is the case or if you are unsure if metal hardware has been used. In such circumstances, the radiologist/radiographer may need to seek further information from your surgeon and/or consider other scanning methods; the risk of MR scanning in such situations could result in patient injury.

Notice regarding any serious incident that occurs in relation to these devices

Report any serious incident (e.g. serious deterioration of a patient's health) that occurs in relation to these devices to the manufacturer (Geistlich Pharma AG) and to the Therapeutics Goods Administration (TGA).

The Therapeutics Goods Administration (TGA) address and website

Therapeutic Goods Administration
PO Box 100
Woden ACT 2606
Australia
https://www.tga.gov.au/

The manufacturer address and website

Geistlich Pharma AG
Bahnhofstr. 40
6110 Wolhusen
Switzerland
www.geistlich-pharma.com

The distributor address and website (Australian sponsor)

Geistlich Pharma Australia Pty Ltd.
The Zenith – Tower A,
Level 21, Suite 21.02
821 Pacific Highway
Chatswood NSW 2067
Australia
Phone +61-(1)-800 776 326
info@geistlich.com.au
www.geistlich.com.au

Date of information: 2021-09

Chondro-Gide® – Bilayer Collagen Matrix

Specifications of Chondro-Gide®

Collagen is the main structural protein of connective tissue and an important component of articular cartilage. Chondro-Gide® is comprised of collagen type I and III. It is manufactured in a patented process which results in a unique bilayer matrix (image 1) with a compact and a porous side.

The compact layer (image 2) consists of a compact, cell occlusive surface, preventing the mesenchymal stem cells from diffusing into the joint space and protecting them from mechanical stress. The porous layer (image 3) of the matrix is composed of loose collagen fibres that support cell invasion and attachment. The arrangement of the fibres provides high tensile strength and resistance to tearing. Chondro-Gide® can therefore be held in position by glue, sutures or pins.

Chondro-Gide® is produced from porcine collagen, which is naturally resorbed. Collagenases, gelatinases and proteinases are responsible for its breakdown into oligopeptides and finally single amino acids.

Safety and Quality

The proprietary manufacturing process of Chondro-Gide® involves several steps before the unique bilayer design is achieved. Standardised processes under clean room conditions, rigorous in-process and end control guarantee a high quality natural product. Thorough biocompatibility safety testing according to international standards proves that all elements possibly causing an undesirable local or systemic response are removed during the manufacturing process. The immunogenic potential of the matrix is reduced to a minimum.

Chondro-Gide® is a CE-marked product to cover articular cartilage defects that are either treated with autologous chondrocyte implantation (ACI) or with bone marrow stimulation techniques (AMIC®).

Image 1: Unique bilayer structure of Chondro-Gide® (100x)

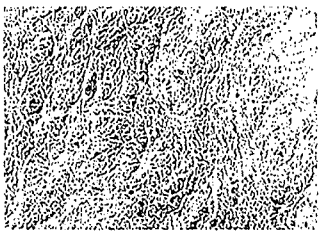


Image 2: Compact, cell occlusive surface (SEM 1500x)

Image 3: Porous, cell adhesive surface (SEM 1500x)

The AMIC® procedure is an easy to handle, cost effective method with good clinical results [3] and is particularly suitable for treating osteochondral and retropatellar defects [4].

Geistlich Surgery

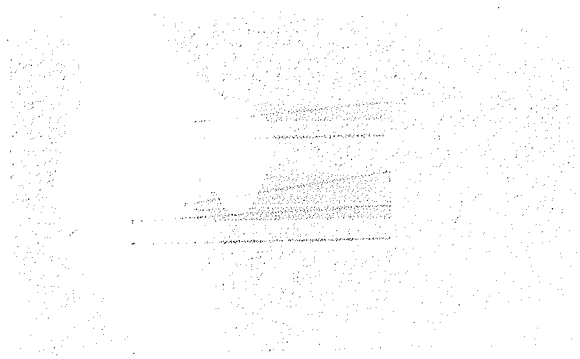
Sustained clinical success following AMIC® Chondro-Gide® treatment of focal cartilage lesions in the knee joint

Summary of the publication by Gille et al. "Autologous Matrix-Induced Chondrogenesis for Treatment of Focal Cartilage Defects in the Knee. A Follow-up Study." in Orthop J Sports Med. February 2021. doi: 10.1177/2325967120981872.

Multisite prospective registry (Level IV):

- Patients with symptomatic, focal cartilage lesions (Outerbridge Grade III/IV) were included
- AMIC® as index procedure – cases requiring concomitant surgery were excluded
- 131 patients with pre- and post-operative data in the registry were available for analysis:
  - Mean age at surgery: 36.6 ± 11.7 years
  - Mean defect size: 3.3 ± 1.8 cm²
  - Mean follow up: 4.6 ± 2.9 years

Location of chondral lesions (n=131):



Sustained clinical improvement after AMIC®

- Significant improvement in median Lysholm (Fig. 1) and KOOS Score (Fig. 2), as well as significant reduction of pain VAS were already seen within the first post-operative year after AMIC®.
- The improvement was maintained up to 7 years.

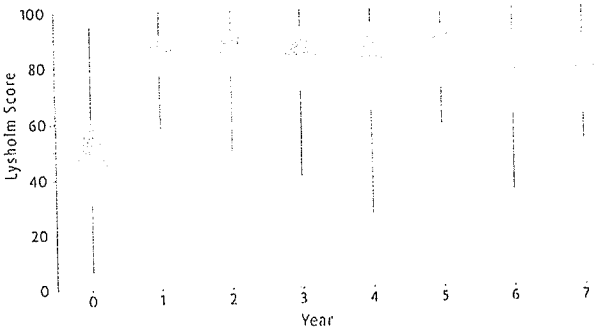


Fig. 1: Lysholm score over time

No effect of patient-specific factors on the results

- Neither age, sex (Fig. 2), previous surgery, defect location, nor defect size had a significant effect on the outcomes.

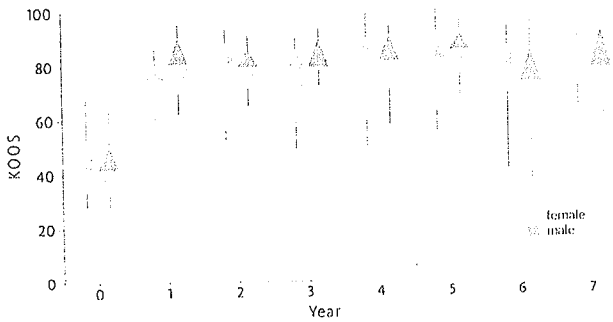


Fig. 2: KOOS score over time per sex

**CHONDRO-GIDE®
LITERATURE HIGHLIGHT**

The bilayer collagen membrane is an established product for cartilage therapies with 20 years of clinical use. AMIC® Chondro-Gide®, a technique that combines bone marrow stimulation with the use of a collagen membrane, has been used for over 15 years. Based on pre-clinical and clinical evidence, AMIC® was included in the treatment recommendations for cartilage lesions of the talus, knee and hip by the respective committees of the German Society for Orthopaedics and Trauma (DGOU).

Recently, the intended use of Chondro-Gide® was extended to augment meniscal repair by wrapping the membrane around the sutured meniscus. The corresponding meniscus wrapping technique is registered as AMMR®.

This literature highlight addresses important aspects of the evidence for the use of Chondro-Gide®.

Conclusions

› The results reported for this study were solely due to the AMIC® treatment, as cases requiring concomitant surgeries at the time of the index procedure were excluded.

› The registry-based study followed the clinic standard without additional, predefined follow-up visits imposed on patients. Although patients were motivated by study staff to complete questionnaires, the number of patients with data at each post-operative time point decreased as time progressed from the index surgery. This is a known limitation of registries and results in data gaps that decrease the power of the statistical analysis.

› AMIC® was an effective treatment for patients with mid-sized Outerbridge grade III/IV cartilage defects in the knee and led to reliably favorable results up to 7 years post-operatively.

For details of the study refer to the original article:

Original Research

Autologous Matrix-Induced Chondrogenesis for Treatment of Focal Cartilage Defects in the Knee

A Follow-up Study

Justus Gille,*† Prof.Dr.med., Ellen Reiss,‡ Cand.med., Moritz Freitag,† Cand.med., Jan Schagemann,† Prof.Dr.med., Matthias Steinwachs,§ Prof.Dr.med., Tomasz Piontek,‖ Prof.Dr.med., and Eric Reiss,‡ Dr.med.

Investigation performed at University of Luebeck, Germany

1. Geistlich Pharma AG, data on file (bench tests and pre-clinical studies)
2. Kramer J, et al., Cell Mol Life Sci. 2006 Mar;63(5):616-26. (Clinical study)
3. Walther M, et al., Oper Orthop Traumatol. 2014 Dec;26(6):603-10. (Clinical Study)
4. Fossum V, et al., Orthop J Sports Med. 2019 Sep 17;7(9). (Clinical Study)
5. Kaiser N, et al., Arch Orthop Trauma Surg. 2020 Aug 13. (Clinical Study)

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The Orthopaedic Journal of Sports Medicine, 7(9). DOI: 10.1177/2325967119865217

Collagen-Covered Autologous Chondrocyte Implantation (ACI-C) versus Autologous Matrix-Induced Chondrogenesis (AMIC®) for Cartilage Repair in the Knee

Vegard Fossum, Ann Kristin Hansen, Tom Wilsgaard, Gunnar Knutsen

› First randomized controlled clinical study (Level 1) comparing clinical outcomes between ACI-C and AMIC® Chondro-Gide® for the treatment of chondral or osteochondral defects in the knee

› At 2 years, both treatment methods resulted in a similar significant improvement in clinical outcomes while no significant superiority of either ACI-C or AMIC® was observed.

Start

› Patients with 1 or 2 chondral or osteochondral lesions of the distal femur and/or patella were randomly assigned to undergo either AMIC® or ACI-C treatment

› Symptomatic defect ≥ 3 cm² was an inclusion criterion.

› All patients had 1-6 prior surgeries in the index knee and 50% had a prior microfracture procedure

At 1 year follow-up

› No treatment failures and no patients were lost-to follow-up

At 2 years follow-up

› Failure was defined as any deterioration in KOOS during the 2 year follow up ("clinical failure") or patients needing a new resurfacing procedure of the index lesion or a total knee replacement (= "hard failure")

41

› Mean age: 37.2 (19-50) years
› 17 patients with 1 defect, 4 with 2 defects
› Mean defect size: 4.9 (1.2-10.5) cm²
› 33% females
› 24% of the cases with Kellgren Lawrence (K-L) grade ≥ 2

› Mean age: 35.3 (24-50) years
› 16 patients with 1 defect, 1 with 2 defects
› Mean defect size: 5.7 (1.2-12) cm²
› 60% females
› 40% of the cases with K-L grade ≥ 2

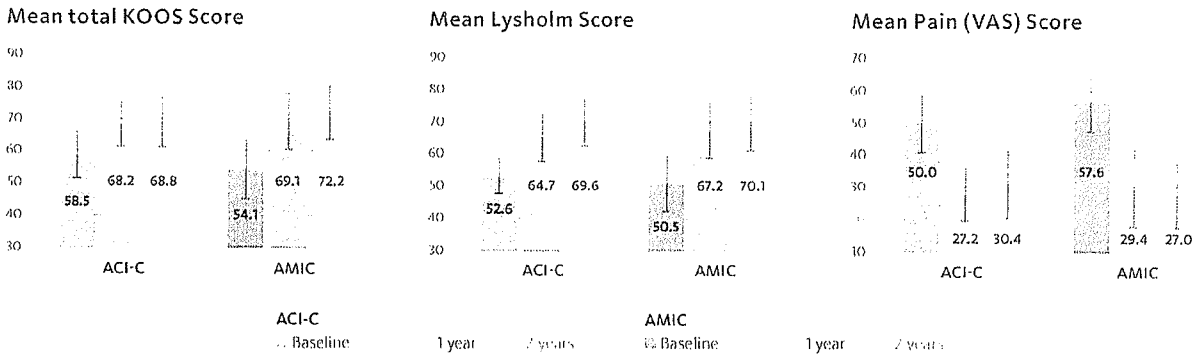
17 AMIC

1 "lost to follow-up"

Significant Improvement of Knee Function (KOOS/Lysholm) and Pain VAS Score

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

› Despite a larger mean defect size and more patients with K-L grade ≥ 2 in the AMIC® group, at 1 and 2 years, this group showed a higher mean improvement in all clinical scores compared to the ACI-C group (see graphs below).



**CHONDRO-GIDE®
LITERATURE HIGHLIGHT**

The bilayer collagen membrane is an established product for cartilage therapies with 20 years of clinical use. AMIC® Chondro-Gide®, a technique that combines bone marrow stimulation with the use of a collagen membrane, has been used for over 15 years. Based on pre-clinical and clinical evidence, AMIC® was included in the treatment recommendations for cartilage lesions of the talus, knee and hip by the respective committees of the German Society for Orthopaedics and Trauma (DGOU).

This literature highlight addresses important aspects of the evidence for Chondro-Gide® and AMIC®.

› Patients with previous microfracture surgery to the study knee exhibited a lower improvement of mean total KOOS, but this difference was not significant.

› At 2 years, there were 3 clinical failures with KOOS deterioration in both groups. In addition, 2 patients in the AMIC® group were classified as "hard failures" with progression to a total knee replacement (both patients with a K-L score of 2 at baseline) while there were none in the ACI-C group.

Conclusions

› These good results at 2 years after AMIC® repair were achieved in **relatively large, degenerative lesions** (mean defect size of 5.2 cm²).

› The **clinical outcomes showed no significant difference in improvement** when comparing the ACI-C and AMIC® group at 2 years, which may be due to the small number of patients in each group resulting in a low power of the study.

› **Cell source** (bone marrow stem cells or expanded autologous chondrocytes) **did not appear to affect** the results of this study.

› The authors concluded that if the results of the study can be confirmed after 5- and 10-year follow-up, **AMIC® could be considered an equal alternative to techniques based on chondrocyte transplantation** for treatment of knee cartilage defects.

› Furthermore, if comparable long-term results are obtained, AMIC® as a one-step procedure would be preferable to the more complex, two-stage ACI-C procedure.

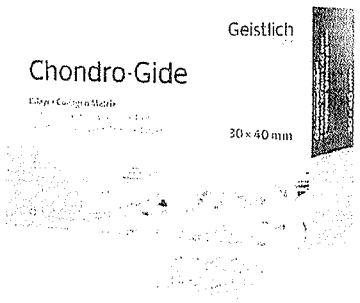
For details of the study refer to the original article:

Collagen-Covered Autologous Chondrocyte Implantation Versus Autologous Matrix-Induced Chondrogenesis

A Randomized Trial Comparing 2 Methods for Repair of Cartilage Defects of the Knee

Vedrad Ivosevic,[†] MD, Ares Kristo Hansen,[‡] MD, PhD, Tom Wikstrand,[†] Prof., and Gunnar Knutsen,[†] MD, PhD
Investigation performed at Department of Orthopaedic Surgery, The University Hospital of North Norway, Tromsø, Norway

› Chondro-Gide®, the original AMIC® membrane[1]
› One-step procedure for cartilage regeneration techniques[2,3]
› With more than 10 years of clinical experience[4]



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1 Geistlich Pharma AG, data on file
2 Schiavone Panni, A. et al. Good clinical results with autologous matrix-induced chondrogenesis (Amic) technique in large knee chondral defects. Knee Surg Sports Traumatol 2018 Apr;26(4):1130-1136. doi: 10.1007/s00167-017-4503-0. (Clinical study)
3 Niemeyer, P. et al. Significance of Matrix-augmented Bone Marrow Stimulation for Treatment of Cartilage Defects of the Knee: A Consensus Statement of the DGOU Working Group on Tissue Regeneration. Z Orthop Unfall 2018; 156(05): 513-532. doi: 10.1055/s-0043-124457
4 Kaiser, R., et al. Clinical results 10 years after AMIC in the Knee. Swiss Med Wkly. 2015; 145 (Suppl 210), 43S. (Clinical study)

Geistlich Surgery

Arch Orthop Trauma Surg. 2020 Aug 13. doi: 10.1007/s00402-020-03564-7.

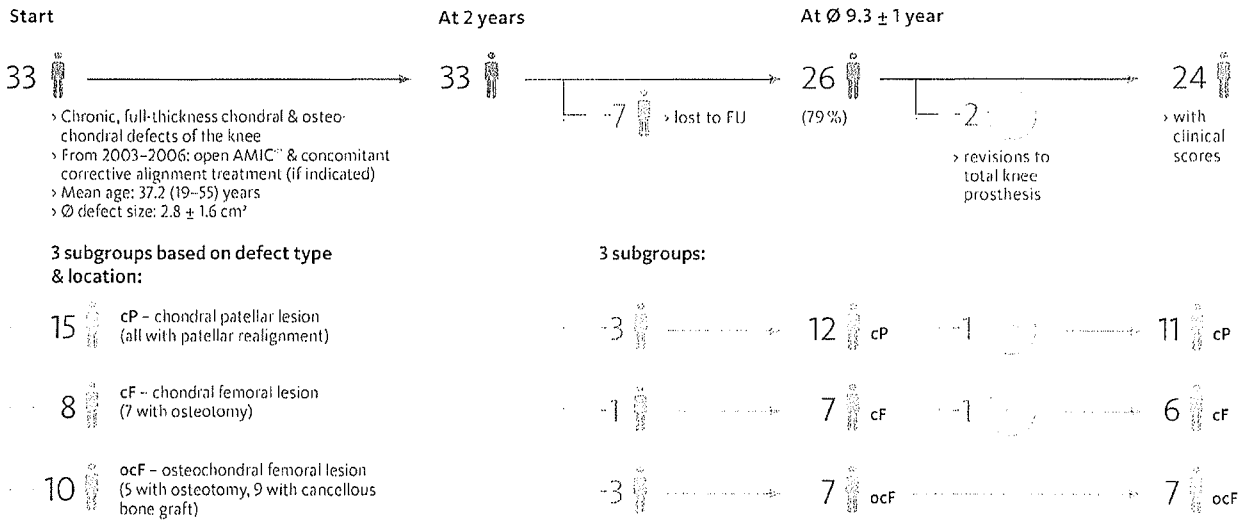
Long-lasting clinical benefits of AMIC® in the aligned knee

Nadine Kaiser, Roland P. Jakob, Geert Pagenstert, Moritz Tannast, Daniel Petek

› AMIC® Chondro-Gide® showed sustained improvement in pain and function at a mean 9.3 ± 1 years for patients with chronic, chondral and osteochondral lesions of the femoral condyles or patella in the aligned knee.

› The study emphasizes the importance of a concomitant lower limb alignment correction for a good long-term outcome, which is particularly of benefit for younger adults with cartilage damage in the knee as well as compartmental overload.

Retrospective single center case series (Level IV):



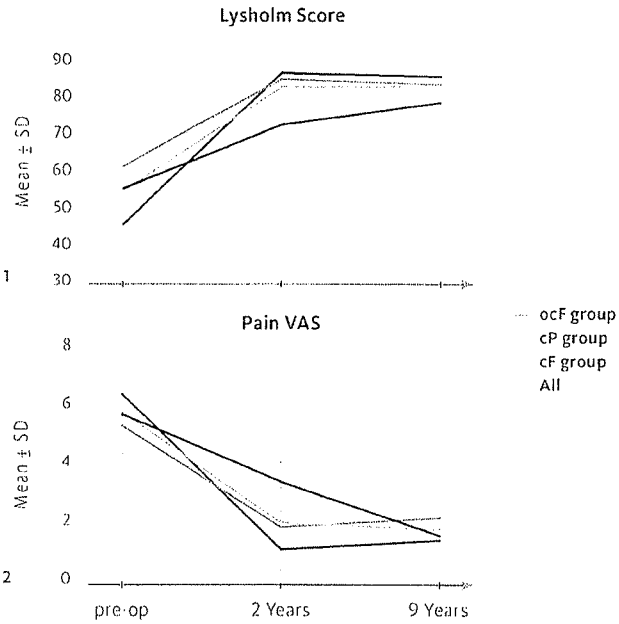
Improvement in Pain and Function after an average of 9.3 ± 1 Years

› Significant improvement in knee function (Lysholm, Fig. 1) and pain VAS (Fig. 2) scores for all subgroups at a mean 9.3 years after AMIC® compared to pre-op.

› 2/26 (7.7%) patients required a total knee prosthesis at 9 and 10 years after the initial AMIC® procedure. Their scores were not included in the final mean scores.

› The **overall mean Lysholm** and **VAS** scores improved significantly from pre-op to 2 years post-op. From 2 to 9 years, no significant differences in the mean scores were observed (Fig. 1 & 2, orange line).

› **Subgroup analysis** revealed significant improvement in Lysholm and pain VAS at 2 years for the cP- and ocF-group compared to pre-op, however not for the cF-group. While the improvement remained stable up to 9 years for these 2 groups, the cF-group continued to improve from 2 to 9 years (Fig. 1 & 2, green line).



Geistlich
Surgery

CHONDRO-GIDE®
LITERATURE HIGHLIGHT

The bilayer collagen membrane is an established product for cartilage therapies with 20 years of clinical use. AMIC® Chondro-Gide®, a technique that combines bone marrow stimulation with the use of a collagen membrane, has been used for over 15 years. Based on pre-clinical and clinical evidence, AMIC® was included in the treatment recommendations for cartilage lesions of the talus, knee and hip by the respective committees of the German Society for Orthopaedics and Trauma (DGOU).

Recently, the intended use of Chondro-Gide® was extended to augment meniscal repair by wrapping the membrane around the sutured meniscus. The corresponding meniscus wrapping technique is registered as AMMR™.

This literature highlight addresses important aspects of the evidence for the use of Chondro-Gide®.

Conclusions

› First study investigating **long-term outcome** after an **AMIC® procedure** for medium-sized cartilage lesions in the knee.

› **Pain and function scores significantly improved** after **AMIC® combined** with a **concomitant realignment** procedure (if indicated per radiologic assessment) and **remained stable up to 10 years** after surgery.

› **Limitations** of the study to be considered: a) heterogeneous patient population with respect to localization and cause of the underlying lesion, b) concomitant procedures performed during AMIC® may confound the results, and c) retrospective design of the single-center study is a known methodological weakness. Despite these limitations, the reported **results are favorable,** as there was a **low revision rate** of 7 % at 9 years.

› Younger patients may especially benefit from a procedure that can delay and potentially prevent the need for an early arthroplasty.

› The study emphasizes the importance of a **combined strategy** with **cartilage repair** and **alignment correction** (where indicated) to achieve a **durable, long-lasting benefit** for the patients.

For details of the study refer to the original article:

Archives of Orthopaedic and Trauma Surgery
https://doi.org/10.1007/s00402-020-03564-7

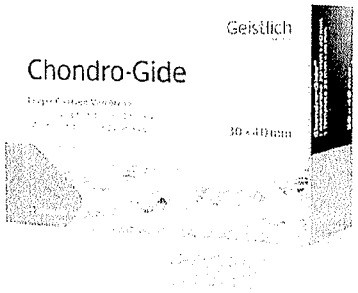
ORTHOPAEDIC SURGERY

Stable clinical long term results after AMIC in the aligned knee

Nadine Kaiser[1] · Roland P. Jakob[2] · Geert Pagenstert[3] · Moritz Tannast[2] · Daniel Petek[2]

Received: 2 February 2020 / Accepted: 2 August 2020

› Chondro-Gide®, the original AMIC® membrane[1]
› One-step procedure for cartilage regeneration techniques[1,2,3]
› With more than 10 years of clinical experience[4]



1 Geistlich Pharma AG, data on file
2 Schiavone Panni, A. et al. Good clinical results with autologous matrix-induced chondrogenesis (Amic) technique in large knee chondral defects. Knee Surg Sports Traumatol 2018 Apr;26(4):1130-1136. doi: 10.1007/s00167-017-4503-0. (Clinical study)
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4 Kaiser, N. et al. Stable clinical long term results after AMIC® in the aligned knee. Arch Orthop Trauma Surg. 2020 Aug 13. doi: 10.1007/s00402-020-03564-7.

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Geistlich Surgery

Cartilage, 2019:1-15. Doi: 10.1177/1947603519870846

Systematic Review and Meta-Analysis of the Clinical Evidence on the Use of Autologous Matrix-Induced Chondrogenesis (AMIC®) in the Knee

Matthias R. Steinwachs, Justus Gille, Martin Volz, Sven Anders, Roland Jakob, Laura De Girolamo, Piero Volpi, Alfredo Schiavone-Panni, Sven Scheffler, Eric Reiss, Udo Wittmann

The first meta-analysis of a one-step cartilage repair procedure in the knee using the Chondro-Gide® membrane demonstrates significant improvement in pain and functional scores compared to pre-operative values during a follow-up of longer than 5 years.

Systematic Literature Search

66 publications were identified in a systematic search performed in the PubMed & Embase databases as well as in other sources by use of the search terms: "Chondro-Gide®", "AMIC®", "cartilage", and "knee".

→ 54 publications were excluded because, among other reasons, the following inclusion criteria were not fulfilled: clinical study with a minimum of 6 patients, cartilage defects in the knee, and primary endpoints of pain and function. None of the excluded studies reported adverse events related to the AMIC® procedure.

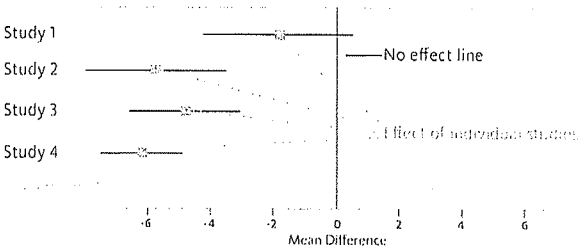
→ **12 publications were included:**
- 375 patients with a minimum follow-up of 2 years
- Mean age: 36.2 years (14-70 years)
- with chondral and osteochondral defects Outerbridge Grade III & IV
- Mean defect size: 4.2 cm² (0.8-22 cm²)

Statistical Methods

- Meta-analysis based on reported pain VAS, Lysholm, and IKDC scores.
- The random-effects model was used for statistical analysis using an estimator as a measure of the heterogeneity between the different studies.
- Results were displayed using Forest plots, which demonstrate the heterogeneity and effect size of the individual studies as well as the [illegible] (see graph on the right).
- The vertical line through 0 indicates no effect: a big distance of the individual effect to this line and a narrow confidence interval indicate a significant treatment effect and conclusive data.

Forest Plot

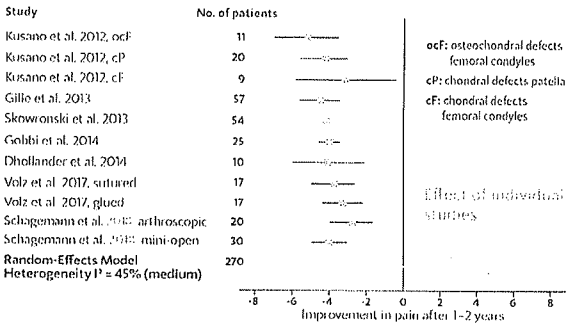
Effect size with 95% confidence interval (——)



Significant and Clinically Relevant Improvement in Pain

- The forest plots on the right indicate a significant improvement of 4.0 points for pain VAS from baseline to follow-up at years 1-2 (see upper graph) and an even bigger improvement of 4.8 points after a follow-up of >3 years (see lower graph).
- This reduction in pain VAS of more than 4 points (on a scale from 0-10) corresponds to a clinically important difference.

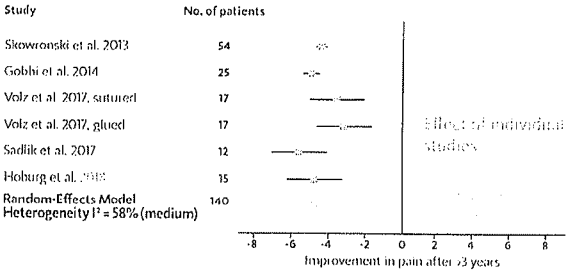
Forest Plot for Pain VAS after 1-2 Years



Functional Improvement (no graph shown)

- The random effects model shows significant improvement for the Lysholm score (by 34.7 points) and IKDC score (by 32.6 points) from baseline to follow-up at years 1-2.
- At follow-up >3 years, the improvement of the IKDC score was even bigger (44.9 points) while the improvement of the Lysholm score remained constant (35.1).

Forest Plot for Pain VAS after >3 Years



**CHONDRO-GIDE®
LITERATURE HIGHLIGHT**

The bilayer collagen membrane is an established product for cartilage therapies with 20 years of clinical use. AMIC® Chondro-Gide®, a technique that combines bone marrow stimulation with the use of a collagen membrane, has been used for over 15 years. Based on pre-clinical and clinical evidence, AMIC® was included in the treatment recommendations for cartilage lesions of the talus, knee and hip by the respective committees of the German Society for Orthopaedics and Trauma (DGOU).

This literature highlight addresses important aspects of the evidence for Chondro-Gide® and AMIC®.

Conclusions

› The meta-analysis documents that the AMIC® Chondro-Gide® procedure significantly improves pain and function in knee joints with chondral and osteochondral lesions.

› The improvement was **maintained over more than 5 years** which confirms the long-term success of AMIC® Chondro-Gide® in Outerbridge grade III & IV lesions with an average size of 4.2 cm^2.

› A conversion to arthroplasty was required in less than 1% (3/375) of the cases. Treatment-related adverse events were not reported, which confirms the **excellent safety profile of the AMIC® procedure.**

› This meta-analysis demonstrates that use of the Chondro-Gide® membrane for coverage of cartilage defects resulted in a significant and durable improvement of clinical outcomes for lesions with an average size of 4.2 cm^2, which is clearly above the size limit for microfracturing.

› Based on the results of this meta-analysis, the authors recommend **AMIC® Chondro-Gide® as the preferred treatment method for knee joints with grade III & IV chondral and osteochondral lesions >2–3 cm^2.**

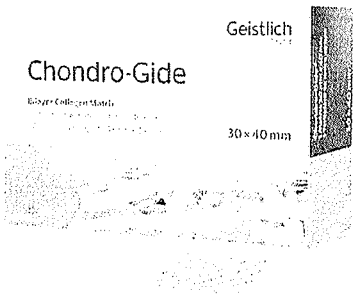
For details of the study refer to the original article:

Original Article

Systematic Review and Meta-Analysis of the Clinical Evidence on the Use of Autologous Matrix-Induced Chondrogenesis in the Knee

Matthias R. Steinwachs [1], Justus Gille [2], Martin Volz [3], Sven Anders [4], Roland Jakob [5], Laura De Girolamo [6], Piero Volpi [7], Alfredo Schiavone-Panni [8], Sven Scheffler [9], Eric Reiss [10], and Udo Wittmann [11]

› Chondro-Gide®, the original AMIC® membrane[1]
› One-step procedure for cartilage regeneration techniques [1,2,3]
› With more than 10 years of clinical experience[4]



1 Geistlich Pharma AG, data on file
2 Schiavone Panni, A. et al. Good clinical results with autologous matrix-induced chondrogenesis (Amic) technique in large knee chondral defects. Knee Surg Sports Traumatol 2018 Apr;26(4):1130-1136. doi: 10.1007/s00167-017-4503-0. (Clinical study)
3 Niemeyer, P. et al. Significance of Matrix-augmented Bone Marrow Stimulation for Treatment of Cartilage Defects of the Knee: A Consensus Statement of the DGOUWorking Group on Tissue Regeneration. Z Orthop Unfall 2018; 156(05): 513-532. doi: 10.1055/a-0591-6457
4 Kaiser, N., et al. Clinical results 10 years after AMIC in the knee. Swiss Med Wkly, 2015. 145 (Suppl 210), 43S. (Clinical study)

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Foot and Ankle Surgery 2020 Aug 15;S1268-7731(20)30164-5. doi: 10.1016/j.fas.2020.07.011.

Systematic Review and Meta-Analysis of the Clinical Evidence Supports the Use of AMIC® in the Ankle Joint

Markus Walther, Victor Valderrabano, Martin Wiewiorski, Federico Giuseppe Usuelli, Martinus Richter, Tiago Soares Baumfeld, Johanna Kubosch, Oliver Gottschalk, Udo Wittmann

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

Systematic Literature Search

[illegible] publications 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: [illegible]
- OCL size varied from [illegible]
- Different surgical approaches and bone marrow stimulation techniques
- Mean follow-up: [illegible] months

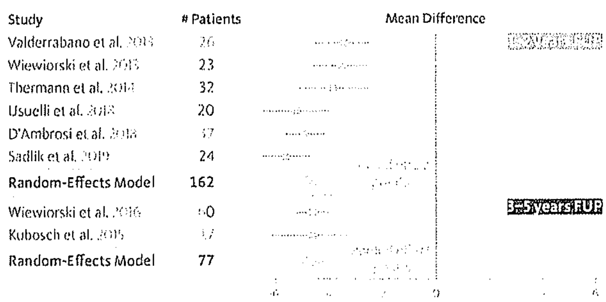
Statistical Methods for Quantitative Analysis

- 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.
- A random effects model was used to evaluate the changes. Results were displayed using forest plots which show the effect of the individual studies (▫) with a 95% confidence interval, as well as the [illegible] ([illegible]).
- The vertical line through 0 indicates no effect: a big distance to the 0-line and a narrow 95% confidence interval for the effect size of an individual study indicate a significant effect and conclusive data.

Improvement in pain following AMIC

- From baseline to 1–2 year follow-up (FUP), the forest plot shows a clinically and statistically significant improvement (reduction) in mean pain of 4.5 points (light blue area).
- From baseline to 3–5 year FUP, mean pain reduced significantly by 4.6 points (light grey area).

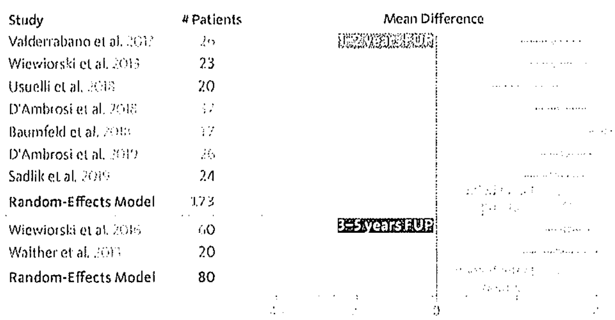
Fig. 1: Improvement in pain compared to baseline



Improvement in joint function following AMIC

- From baseline to 1–2 year FUP, the forest plot shows a significant improvement in mean AOFAS of 31.6 points (light blue area).
- From baseline to 3–5 year FUP, significant improvement was observed for the mean AOFAS by 32.5 points (light grey area) and for the mean FFI by 31 points (not shown).

Fig. 2: Improvement in AOFAS compared to baseline



CHONDRO-GIDE®
LITERATURE HIGHLIGHT

The bilayer collagen membrane is an established product for cartilage therapies with 20 years of clinical use. AMIC® Chondro-Gide®, a technique that combines bone marrow stimulation with the use of a collagen membrane, has been used for over 15 years. Based on pre-clinical and clinical evidence, AMIC® was included in the treatment recommendations for cartilage lesions of the talus, knee and hip by the respective committees of the German Society for Orthopaedics and Trauma (DGOU).

Recently, the intended use of Chondro-Gide® was extended to augment meniscal repair by wrapping the membrane around the sutured meniscus. The corresponding meniscus wrapping technique is registered as AMMR™.

This literature highlight addresses important aspects of the evidence for the use of Chondro-Gide®.

Conclusions

- › The **AMIC Chondro-Gide** procedure for treatment of OCL of the talus provided clinically relevant and **significant improvement** in ankle joint **pain** and **functional outcome** scores **up to 5 years** after surgery.
- › There were **no reported adverse events** or **complications** directly **related** to the **AMIC procedure**. Within the follow-up period, 6 of 492 treated patients (1.2%) required revision surgeries due to persistent pain caused by arthrofibrosis or hypertrophic scar tissue or because of progressive degeneration.
- › None of the patients required conversion to ankle fusion or arthroplasty.
- › Surgical approach and bone marrow stimulation technique were not related to clinical outcome.

For details of the study refer to the original article:

Is there clinical evidence to support autologous matrix-induced chondrogenesis (AMIC) for chondral defects in the talus? A systematic review and meta-analysis

Markus Walther[a,*], Victor Valderrabano[b], Martin Wiewiorski[c], Federico Giuseppe Usuelli[d], Martinus Richter[e], Tiago Soares Baumfeld[f], Johanna Kubosch[g], Oliver Gottschalk[h,a], Udo Wittmann[i]

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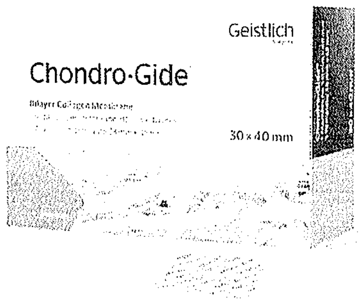
[b] Swiss Ortho Center Schmerzklinik Basel, Swiss Medical Network, Hirschgässlein 15, 4010 Basel, Switzerland
[c] Kantonsspital Winterthur, Zeughausstrasse 71, 8400 Winterthur, Switzerland
[d] Istituto Ortopedico Galeazzi, IRCCS - Unità Specialistica Piede e Caviglia, Foot and Ankle Department, Italy
[e] Klinik für Foot and Ankle Surgery, Rummelsberg 71, 90592 Schwarzenbruck, Germany
[f] Hospital Felício Rocho, Department of Orthopaedics, Av. do Contorno, 9530 Belo Horizonte, MG, Brazil
[g] Department of Orthopedics and Trauma Surgery, Medical Center, Albert-Ludwigs-University of Freiburg, Faculty of Medicine, Albert-Ludwigs-University of Freiburg, Hugstetter Strasse 55, 79106 Freiburg, Germany
[h] Department of General, Trauma and Reconstructive Surgery, University Hospital, LMU, Munich, Germany
[i] Consult AG, Traubstrasse 10, 8050 Zurich, Switzerland

ARTICLE INFO

ABSTRACT

Article history:
Received 10 May 2020

- › Chondro-Gide®, the original AMIC® membrane[1]
- › One-step procedure for cartilage regeneration techniques[1-3]
- › With more than 10 years of clinical experience[4]



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1 Geistlich Pharma AG, data on file
2 Schiavone Panni, A. et al. Good clinical results with autologous matrix-induced chondrogenesis (Amic) technique in large knee chondral defects. Knee Surg Sports Traumatol Arthrosc. 2018 Apr;26(4):1130-1136. doi: 10.1007/s00167-017-4503-0. (Clinical study)
3 Niemeyer, P. et al. Significance of Matrix-augmented Bone Marrow Stimulation for Treatment of Cartilage Defects of the Knee: A Consensus Statement of the DGOU Working Group on Tissue Regeneration. Z Orthop Unfall 2018; 156(05): 513-532. doi: 10.1055/a-0591-6457
4 Kaiser, N. et al. Stable clinical long term results after AMIC® in the aligned knee. Arch Orthop Trauma Surg. 2020 Aug 13. doi: 10.1007/s00402-020-03564-7

Geistlich Surgery

Am J Sports Med., 2019 Jun;47(7):1679-1686. doi: 10.1177/0363546519841574.

Autologous Matrix-Induced Chondrogenesis for Osteochondral Lesions of the Talus: A Clinical and Radiological 2- to 8-Year Follow-up Study

Lizzy Weigelt, Rebecca Hartmann, Christian Pfirrmann, Norman Espinosa, and Stephan H. Wirth

Isolated AMIC® Chondro-Gide® repair in osteochondral lesions of the talus led to significant pain reduction, recovery of ankle function and successful return to sports after a mean follow-up of 4.7 years.
The results for VAS pain, Tegner or AOFAS scores were independent of follow-up duration (< or > 5 years), lesion size (< 1.5 cm² or >1.5 cm²) or the need for subchondral bone grafting.

Retrospective case series (Level IV):

All patients with osteochondral talar lesions treated with an AMIC® procedure between 2009–2016

→ with concomitant procedures

Patients with **isolated** AMIC® procedures

→ Lost to Follow-up

Available for follow-up between August 2017–March 2018

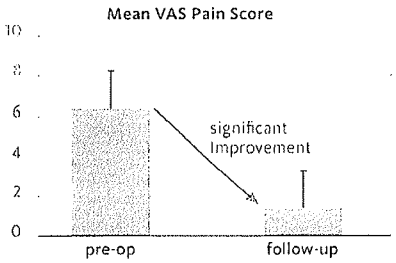
Surgical approach via medial malleolar osteotomy

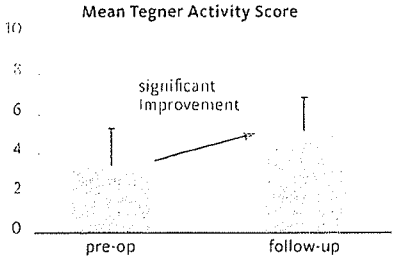
Minimum	mean	maximum
2 years	4.7 years	8 years

- mean age: 35.1 years (range, 15–75 years)
- mean pre-op lesion size: 0.9 ± 0.5 cm² (range, 0.4–2.3 cm²)
- 85% of patients treated with concomitant autologous subchondral bone grafting

Good to excellent results at a mean follow-up of 4.7 years:

- Significant improvement of Pain (VAS) and Sports Activity (Tegner) scores (refer to graphs on the right)
- 79% of patients fully returned to previous sports activity levels
- Mean AOFAS score for ankle function of 93.0 ± 7.5 points
- Moderate radiological results with an average MOCART score of 60.6 ± 21.2 points
- Complete defect filling in 88% of the cases
- No post-operative complications and no revisions for a failed AMIC® procedure





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CHONDRO-GIDE®
LITERATURE HIGHLIGHT

The bilayer collagen membrane is an established product for cartilage therapies with 20 years of clinical use. AMIC® Chondro-Gide®, a technique that combines bone marrow stimulation with the use of a collagen membrane, has been used for over 15 years. Based on pre-clinical and clinical evidence, AMIC® was included in the treatment recommendations for cartilage lesions of the talus, knee and hip by the corresponding committees of the German Society for Orthopaedics and Trauma (DGOU).

This literature highlight addresses important aspects of the evidence for Chondro-Gide® and AMIC®.

Conclusions:

- Isolated AMIC® Chondro-Gide® repair in osteochondral lesions of the talus led to significant pain reduction, improvement in ankle function and successful return to previous sports levels during a follow-up of 2 to 8 years.
- Clinical outcomes did not deteriorate over time and were independent of lesion size, follow-up duration or subchondral bone grafting.
- Moderate MRI findings did not correlate with the good clinical outcome and interpretation of post-operative imaging remains difficult.
- AMIC® Chondro-Gide® is a safe and effective procedure for the treatment of osteochondral lesions of the talus.

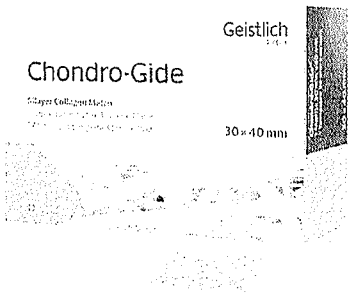
For details of the study refer to the original article:

Autologous Matrix-Induced Chondrogenesis for Osteochondral Lesions of the Talus

A Clinical and Radiological 2- to 8-Year Follow-up Study

Lizzy Weigelt,*[1] MD, Rebecca Hartmann,[1] MD, Christian Pfirrmann,[1] MD, Norman Espinosa,[3] MD, and Stephan H. Wirth,[1] MD
Investigation performed at University Hospital Balgrist, Zurich, Switzerland

- Chondro-Gide®, the original AMIC® membrane[1]
- One-step procedure for cartilage regeneration techniques[2,3]
- With more than 10 years of clinical experience[4]



1 Geistlich Pharma AG, data on file
2 Schiavone Panni, A., et al. Knee Surg Sports Traumatol 2013 Apr;26(4):1130-1136. doi: 10.1007/s00167-017-4503-0. (Clinical study)
3 Niemeyer, P., et al. Significance of Matrix-augmented Bone Marrow Stimulation for Treatment of Cartilage Defects of the Knee: A Consensus Statement of the DGOU Working Group on Tissue Regeneration. Z Orthop Unfall 2018; 156(05): 513-522 doi: 10.1055/a-0591-6457
4 Kaiser, N., et al. Clinical results 10 years after AMIC in the knee. Swiss Med Wkly. 2015; 145 (Suppl 210), 43S. (Clinical study)

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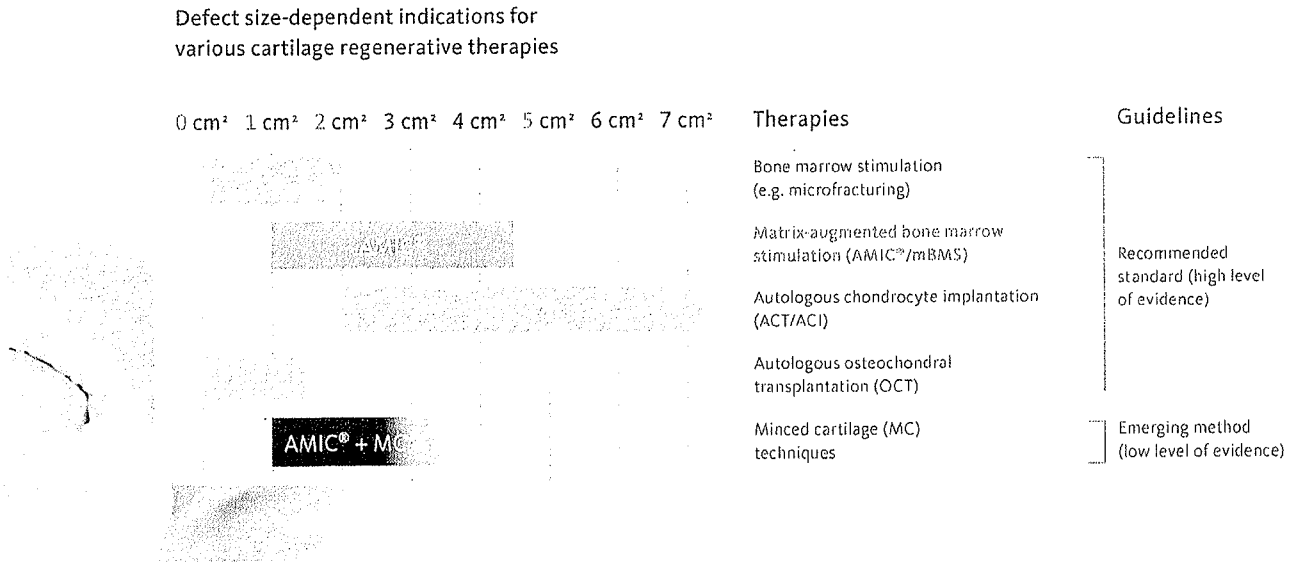
In *Z Orthop Unfall*. 2022. doi:10.1055/a-1663-6807

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

Authors

Philipp Niemeyer, Dirk Albrecht, Matthias Aurich, Christoph Becher, Peter Behrens, Peter Bichmann, Gerrit Bode, Peter Brucker, Christoph Erggelet, Marco Ezechieli, Svea Faber, Stefan Fickert, Jürgen Fritz, Arnd Hoburg, Peter Kreuz, Jörg Lützner, Henning Madry, Stefan Marlovits, Julian Mehl, Peter E Müller, Stefan Nehrer, Thomas Niethammer, Matthias Pietschmann, Christian Plaass, Philip Rössler, Klaus Rhunau, Bernhard Schewe, Gunter Spahn, Matthias Steinwachs, Thomas Tischer, Martin Volz, Markus Walther, Wolfgang Zinser, Johannes Zellner, Peter Angele



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

New features compared to previous guidelines

- Matrix-augmented bone marrow stimulation (mBMS), such as the AMIC® procedure, has been included in the recommendation as a standard method for treatment of chondral defects from 1–4.5 cm² as well as for osteochondral defects from 0–4 cm².
- For the first time, a subdivision in recommended standard methods and methods with potential but not yet sufficient scientific evidence was made.
- For these recommendations, a strict separation of purely chondral and osteochondral defects with separately assigned suitable treatment options was introduced.
- Focal degenerative cartilage damage was classified as suitable for surgical treatment.
- An axial deviation >5° remains a contraindication for cartilage regenerative therapy despite a trend to correction of even smaller deviations.
- ICRS grade I and II lesions on corresponding joint surfaces are no longer considered a contraindication even without supplementary treatment.
- Cartilage regenerative surgery in case of substantially reduced meniscal tissue continues to be classified as critical.

CHONDRO-GIDE®
LITERATURE HIGHLIGHT

This literature highlight addresses important aspects of the evidence for the use of Chondro-Gide®.

XPERIENCE EVIDENCE

100+ peer-reviewed publications

AMIC® Chondro-Gide®

- Combines bone marrow stimulating techniques with the collagen membrane[1]
- Compatible with a range of cost-efficient, one-step cartilage regeneration techniques[2]
- Stable results over 10+ years[3]
- More than 15 years of clinical success
- Biocompatible and naturally resorbed[1]

1 Geistlich Pharma AG, data on file (bench tests and pre-clinical studies)
2 Kramer J, et al., *Cell Mol Life Sci.* [illegible] (Clinical study)
3 Walther M, et al., *Oper Orthop Traumatol.* [illegible] (Clinical study)
4 Fossum V, et al., *Orthop J Sports Med.* [illegible] (Clinical study)
5 Kaiser N, et al., *Arch Orthop Trauma Surg.* [illegible] (Clinical study)

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Cartilage Treatment with AMIC®

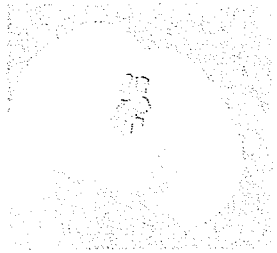
Regenerative Therapy for Cartilage Defects

Patient Guide

swiss made


more restrictions."
Results can vary depending on a patient's age, health, and other factors.

About Cartilage



Cartilage is a strong and flexible tissue that covers the surface of the bones in a joint. It provides cushioning and a smooth, lubricated layer between the bones. But unlike skin or muscle tissue, it does not have blood vessels or nerves. That means it has very limited ability to repair itself. If not treated, a defect can grow larger over time, leading to osteoarthritis.

How Cartilage is Damaged

Cartilage damage can result from a trauma or injury, such as a fall during sports activities. It can also be caused by imperfect alignment or instability of the joint. Or it can simply happen because of wear and tear. Minor injuries may heal over a few weeks or months, but more serious damage can often require surgery.

Treatment

Treatment depends on many factors, such as the size and location of the defect, your biological age, general health status and activity levels. The goal is always to repair the cartilage, alleviate pain, restore joint function, and prevent the progression of damage.

HANNA'S STORY

In 2015, Hanna fell while horseback riding and damaged the cartilage in her knee. Her surgeon recommended arthroscopic surgery with AMIC® to repair her knee.

Since the surgery, Hanna has resumed her active lifestyle. She practices yoga and enjoys horseback riding once again. She is now pain free and her knee is fully functional.

About AMIC®

AMIC is short for Autologous Matrix-Induced Chondrogenesis, meaning that a membrane (in this case made of collagen fibers) supports the body's own healing potential to repair cartilage. AMIC was developed for regenerative therapies that support the body's own healing potential and aim to restore joint function. It is used to repair damaged cartilage in the knee, ankle and hip.

What Happens During AMIC

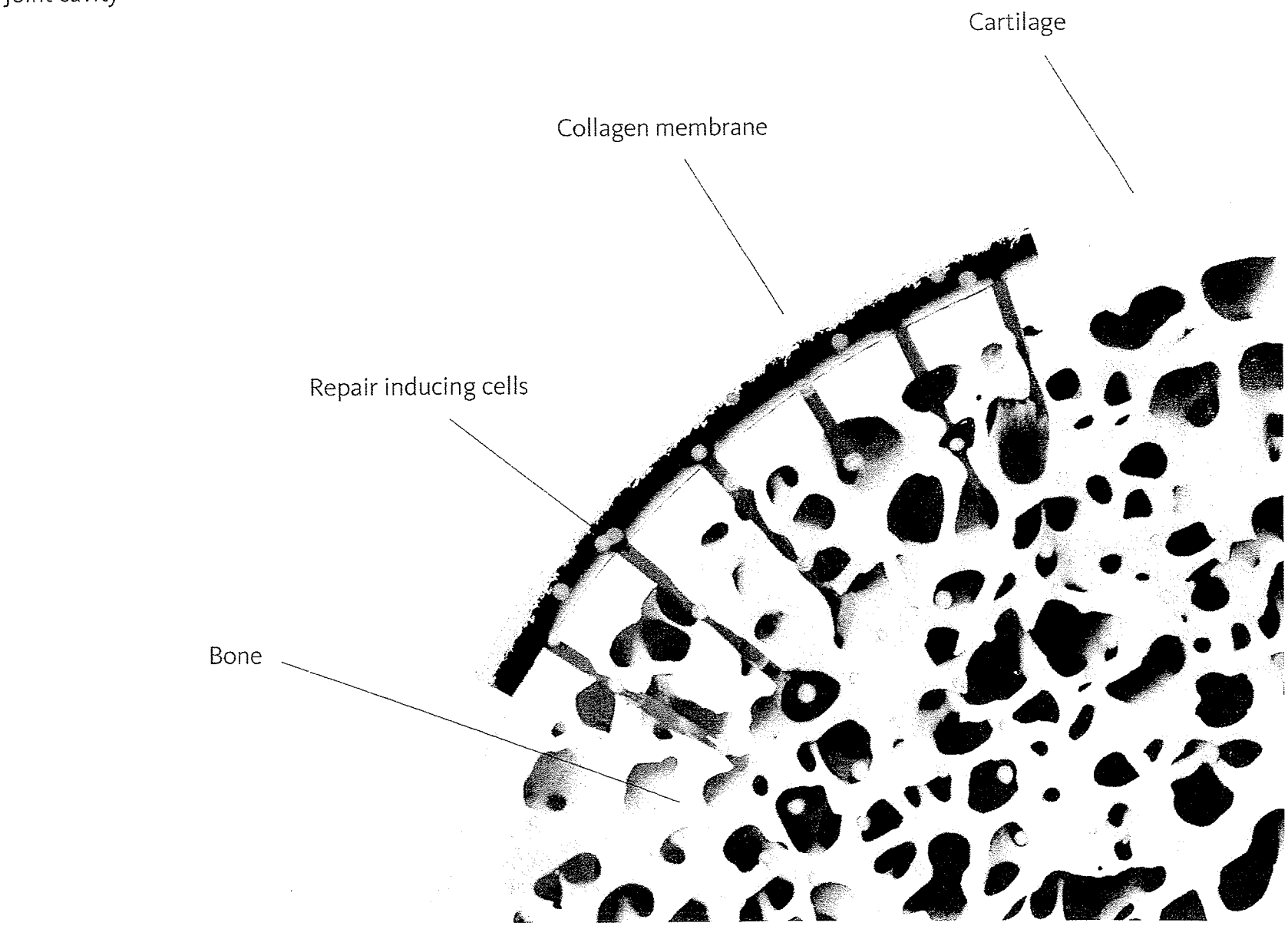
During AMIC, damaged cartilage is removed. Cells from the underlying bone are released into the defect where they promote the growth of new tissue. A small piece of collagen membrane is used to cover the area and protect the new forming tissue from substances and forces in the joint.

A Special Collagen Membrane

The collagen membrane used with AMIC is made in Switzerland from natural collagen material sourced from pigs. Collagen is one of the major building blocks of bones, skin, muscles, tendons, and cartilage. During the manufacturing process, the collagen fibers are isolated, and a flexible but resistant membrane is produced. Over time, the membrane is resorbed by the body and replaced by newly formed tissue.

Positive, Lasting Results

AMIC is backed by more than 10 years of positive clinical results. Developed by Geistlich Surgery in collaboration with leading orthopedic surgeons in Europe, AMIC is a minimally-invasive, 1-step treatment to repair cartilage lesions, alleviate or prevent pain, and slow the progression of joint degeneration.


Joint cavity
Cartilage
Collagen membrane
Repair inducing cells
Bone

AMIC® Knee Surgery – What to Expect

Here are answers to some common questions about AMIC knee surgery. If you have other questions, please talk to your surgeon.

Will I need to be hospitalized for the surgery?

Your AMIC operation will be performed during a short hospital stay. Before the procedure, your doctor will talk you through the possible risks of the operation.

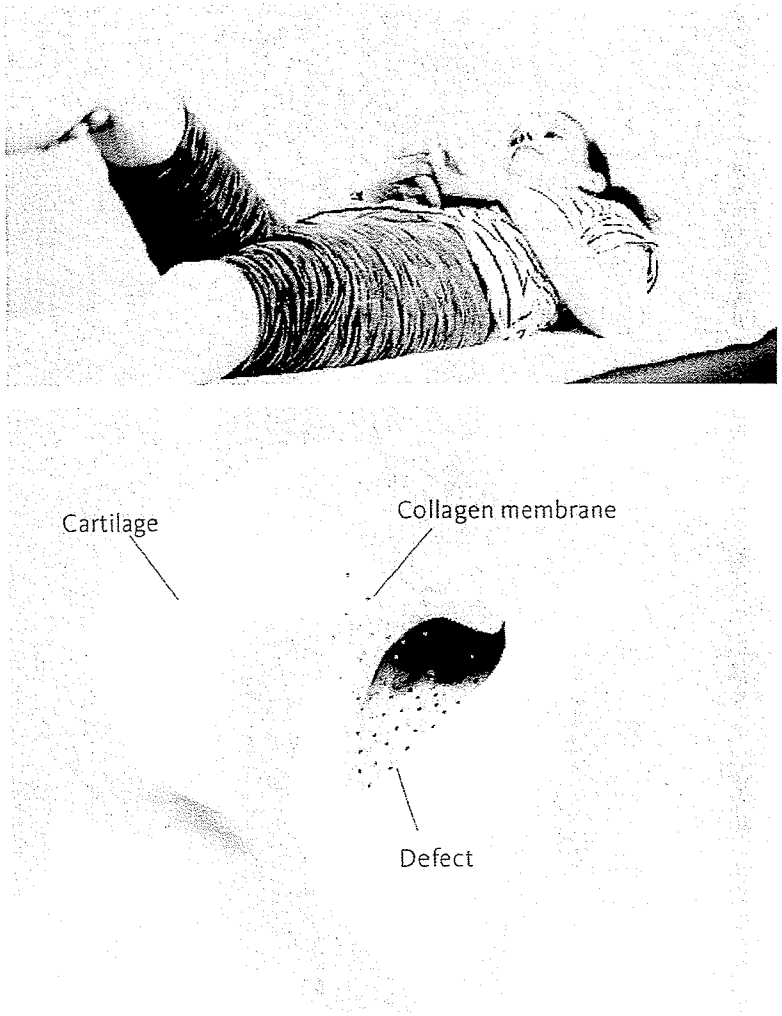
Will I be under anesthetic during the operation?

Yes. You will also meet with an anesthesiologist, who will discuss your anesthesiology options (general, spinal, or local) with you, and then recommend the most suitable option.

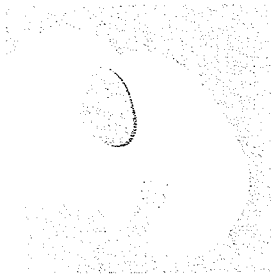
When can I do sports activities again?

After 3 months, you should be able to resume light sports activities such as walking, swimming, and cycling. However, healing times vary, depending on each person's age, general health, and other factors.

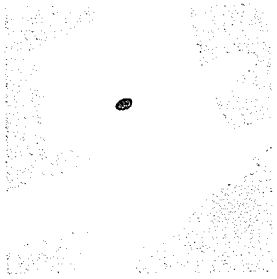
For more details and a sample rehabilitation timeline, please see page 6, "AMIC Knee Surgery Rehabilitation."



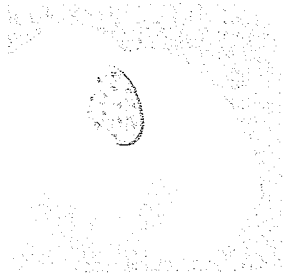
AMIC® Knee Surgery Step-by-Step



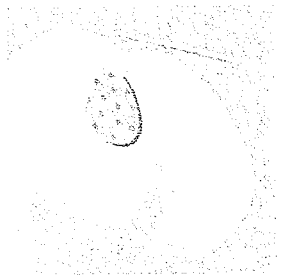
Preparing the Damaged Area
The damaged cartilage is removed.



Trimming the Membrane
The defect is measured and the collagen membrane is trimmed to fit the damaged area.

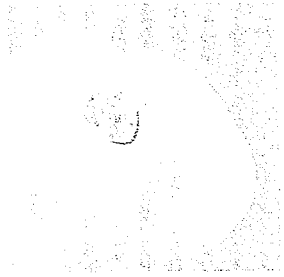


Perforating the Bone
Several tiny holes are made in the bone to release cells.



Applying the Glue
A special type of glue is applied directly to the bone.

In some cases the membrane can also be sutured.



Positioning and Affixing the Membrane
The membrane is placed into the damaged area. The surgeon checks the position of the membrane and then closes the wound.

AMIC® Knee Rehabilitation

Your doctor will create a post-treatment plan that is tailored to your individual needs and also based on the specifics of your operation (e.g., the size and location of the damaged cartilage). The plan outlined below is just an example of what you can expect.

Phase I: Limited Movement

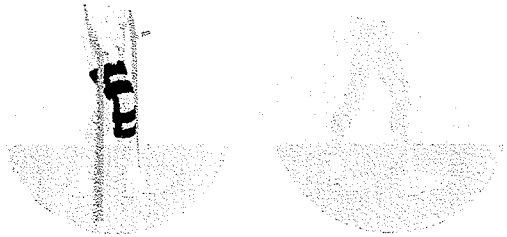
For the first few days after the operation, your knee will be immobilized in a splint. Your doctor will prescribe pain relievers and possibly, cooling therapy, manual lymphatic drainage, or compression therapy to reduce swelling. Later on, your leg will be put in a brace and a physiotherapist will show you how to walk using forearm crutches. You'll need to make sure you keep your full weight off your leg.

Phase II: Regaining Mobility

Your physiotherapist will focus on moving your knee joint in a targeted manner to rebuild the muscles and gradually restore joint mobility. You may also use a continuous passive motion

Immediately After Surgery
Your leg will be immobilized in a splint. Your doctor will prescribe pain relievers and other measures to alleviate swelling.

A Few Days After Surgery
Physiotherapy begins. In physiotherapy, your therapist will gently move your knee.



2 Weeks–3 Months
If you keep your full weight off your leg, you can walk with crutches and gradually increase the amount of weight you put on your leg until full weight bearing is possible.

(CPM) machine to move your knee gently and repeatedly. Your therapy plan will depend on the location and size of the cartilage damage. Some cartilage defects require a longer period of restricted movement than others. Your surgeon will tell you whether you will need to wear a knee brace that restricts the movement of the joint and can be adapted to the healing phase.

Phase III: Returning to Sports Activities

Increased load will help to train your muscles and improve joint function. To further improve your performance and joint function, do the exercises assigned by your physiotherapist diligently. Discuss with your doctor when you can resume specific sports. The newly-formed tissue typically takes 6 to 9 months to mature to the point where you can do more intensive sports.

3–6 Months
Low-impact sports such as walking, swimming, and cycling are possible. You can gradually increase your sports activities.

6–9 Months
You can resume sports like jogging, cross-country skiing, or downhill skiing.

After 9 to 12 Months
You can resume high-impact and contact sports like soccer, basketball or karate.

AMIC® Ankle Surgery – What to Expect

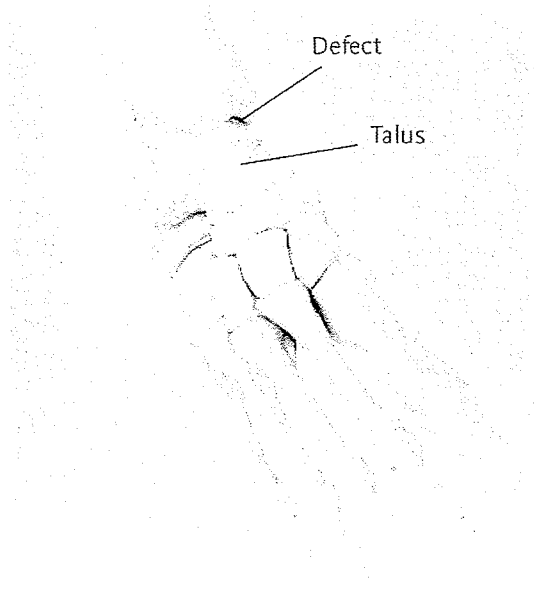
Here are answers to some common questions about AMIC ankle surgery. If you have other questions, please talk to your surgeon.

Will I need to be hospitalized for the surgery?

Your AMIC operation will be performed during a short hospital stay. Before the procedure, your doctor will talk you through the possible risks of the operation.

Will I be under anesthetic during the operation?

Yes. You will also meet with an anesthesiologist, who will discuss your anesthesiology options (general, spinal, or local) with you, and then recommend the most suitable option.



When can I do sports activities again?

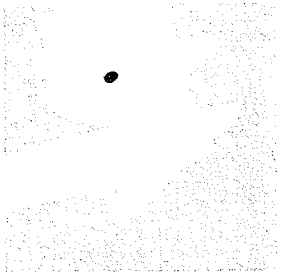
After 3 months, most AMIC ankle patients are able to resume light sports activities such as walking, swimming, and cycling. However, healing times vary, depending on each person's age, general health, and other factors.

For more details and a sample rehabilitation timeline, please see page 10, "AMIC Ankle Surgery Rehabilitation."

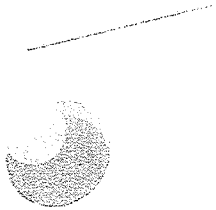
AMIC® Ankle Surgery Step-by-Step

Preparing the Damaged Area
The damaged cartilage and loose pieces of tissue in the joint are removed.

Perforating the Bone
Several tiny holes are made in the bone beneath the cartilage to release cells. If there is bone damage as well, the damaged bone will be removed. A bone graft or bone substitute will be used to rebuild the bone up to the level of the damaged cartilage.



Trimming the Membrane
The defect is measured and the collagen membrane is trimmed to fit the damaged area.



Applying the Glue
A special type of glue is applied directly to the bone beneath the cartilage.

Affixing the Membrane
The membrane is placed into the damaged area. The surgeon checks the position of the membrane and then closes the area.

Creating the necessary space
Depending on the size and location of the defect, the surgeon might need to gain access to the lesion by cutting through the bony prominence of the shin bone. The surgeon will later re-attach it with screws and carefully close the skin.

AMIC® Ankle Rehabilitation

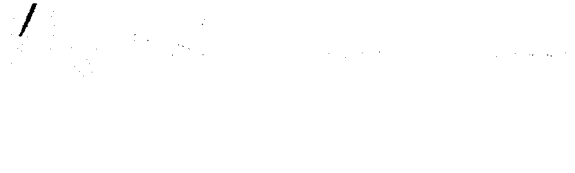
After the operation, your doctor will prescribe medication to help reduce pain and swelling. You will spend a few days in the hospital after the operation. During this time, your leg will be elevated to counteract swelling.

Your doctor will create a personalized rehabilitation plan that reflects your individual needs. To ensure optimal results from your operation, following your doctor's instructions is critical. The plan outlined below is just an example of what you can expect.

Phase I: Limited Movement

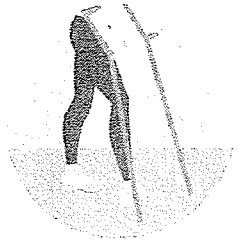
During the first 2-6 weeks after surgery, put only a little weight on your leg. Use forearm crutches to bear most of your weight. Your ankle will be protected by a plaster splint or a stable bandage, depending on what your doctor has found during surgery.

You can move your ankle up and down slightly. But avoid tilting it sideways. Your doctor may also prescribe physiotherapy and manual lymphatic drainage to support the healing process. In physiotherapy, your therapist will gently bend and straighten your ankle.



Immediately After Surgery
Your ankle will be immobilized in a splint or bandaged. Your doctor will prescribe pain relievers and measures to alleviate swelling.

2–6 weeks
You can walk with crutches if you keep your full weight off your leg. Passive movement of your ankle in physiotherapy will help to increase your mobility.



6 weeks–3 months
You can gradually increase the amount of weight you put on your ankle.

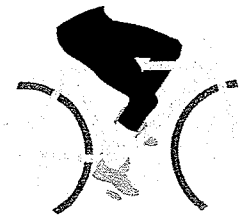
Phase II: Regaining Mobility

After 6 weeks, you can start to put more weight on your ankle. Over 12 weeks, you can gradually increase the load on your ankle to your full weight. Your physiotherapist will show you how to gauge and slowly increase the weight on your leg. Focus on increasing the load gradually. Physiotherapy will help increase your mobility. But you cannot do any sports at this time.

After 3 months, you should be able to go about your everyday activities without forearm crutches. You can cycle or swim. An ankle brace might help you feel more secure. If your ankle is still prone to swelling, try wearing a compression stocking.

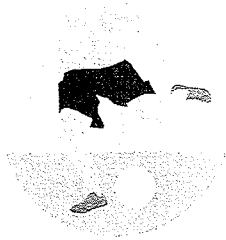
Phase III: Returning to Sports Activities

Cartilage healing depends on many factors besides surgery (e.g., age, weight, medication, metabolism). Full recovery can take 6–24 months. During this phase, you can increase your sports activities. But listen to your body. If you have increased pain, that means you might be putting too much strain on your newly repaired cartilage. In most cases, it's wise to avoid high-impact sports (e.g., jogging, tennis, squash, soccer) for 12 months after surgery. Before you increase your sports activities, consult with your doctor.



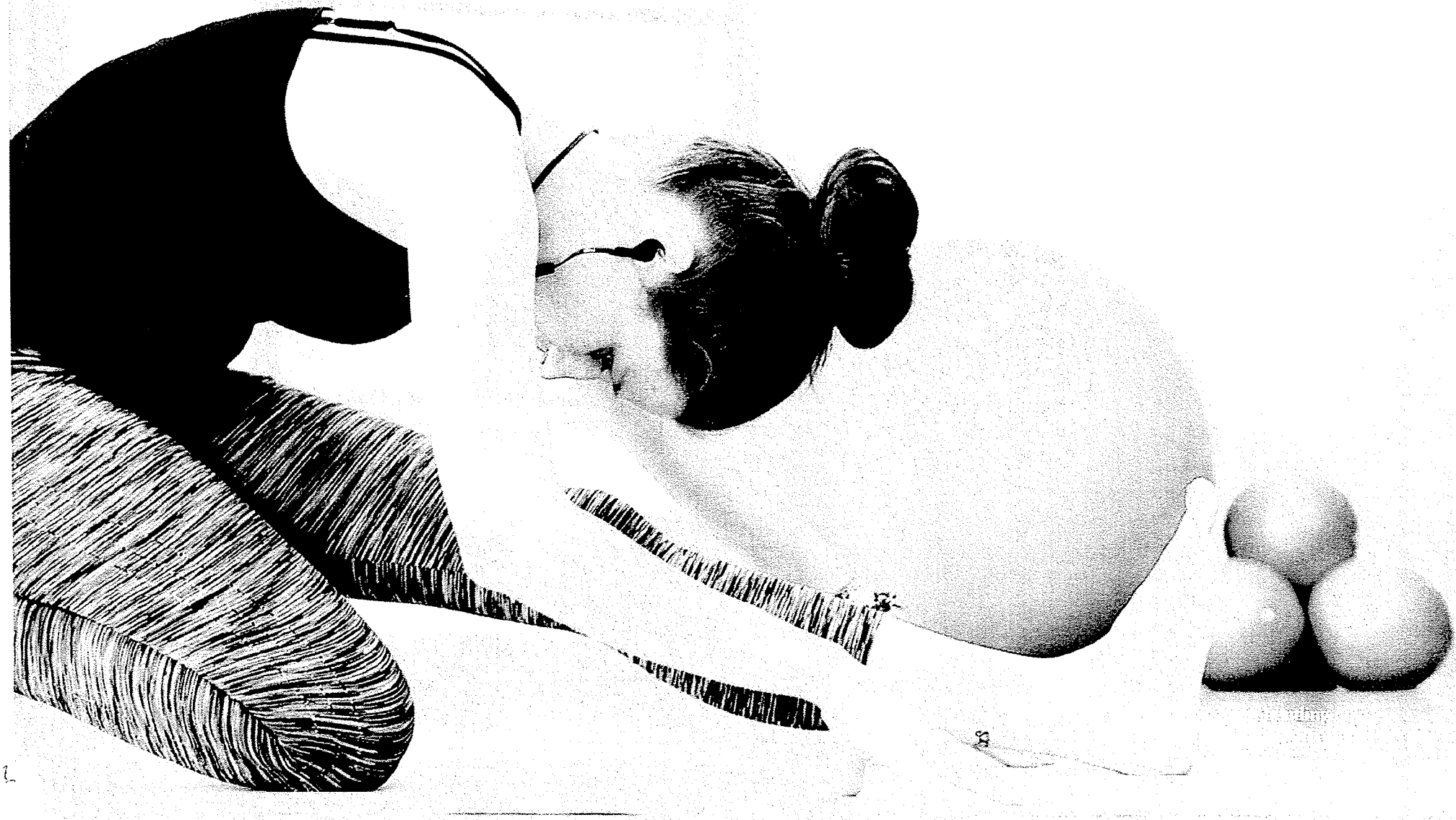
3–6 months
You can walk without crutches. Low-impact sports such as walking, swimming, and cycling are possible.

6–12 months
You can safely increase your sports activities. Ideally, focusing on low-impact sports such as walking, hiking, and cycling.



After 12 months
You can resume high-impact and contact sports like soccer, basketball, tennis and jogging.

"I do yoga and horseback riding, and am physically active without having any problems." Hanna Laura Müller, AMIC® knee patient



For more information visit the
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www.geistlich-surgery.com

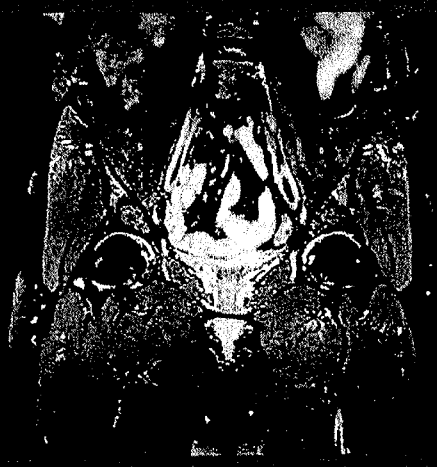
Geistlich
Surgery

Geistlich
Surgery

AMIC® Chondro-Gide® in the Hip

More than
10 Years of Clinical
Experience

swiss made



Preoperative MRI of the right hip with evidence of a chondrolabral separation and adjacent cartilage damage to the acetabulum. Image courtesy of Dr. Wolfram Steens

Chondral defects in the hip, whether acute or chronic, can cause severe dysfunction and joint pain. Trauma, osteonecrosis, labral tears, and loose bodies are among the many possible causes. In addition, femoralacetabular impingement (FAI) is one of the most common causes of localized cartilage defects and damage requiring hip arthroscopy.[1]

Damaged cartilage has limited capacity to heal itself. If left untreated, the damage can worsen over time. With minimally-invasive arthroscopic treatment approaches for chondral defects in the hip, it is now possible to preserve the hip-joint cartilage and delay or possibly even avoid total hip replacement surgeries[1]. One such treatment approach is AMIC® Chondro-Gide® in the hip.

Correct diagnosis of cartilage defects in the hip is challenging. A patient's medical history can provide pointers to a cartilage defect, if symptoms have persisted for a long time. However, they tend to be heterogeneous in early phases.[2]

The differential diagnosis of cartilage defects in the hip is based on physical examination, followed by radiography and magnetic resonance imaging (MRI). It can be extended to include computed tomography (CT) scans and ultrasonography[1,3]. Arthroscopy is the gold standard when determining the location, size, and depth of the defect and also the surrounding bone and soft tissue, particularly the labrum.

Different classification systems are used to describe the location and grade of the lesion. Haddad combines the anatomical location with the morphological grading of the lesion. The modified classification by Griffin provides a more precise definition of its location.

Debridement and microfracture (MFx) are widely accepted treatments for chondral defects in the hip. Janelli et al. describe debridement as the preferred method for patients with a grade one or two chondral defect. MFx is indicated for focal and contained lesions, typically less than 2 cm^2 in size.[3] AMIC Chondro-Gide is indicated for full-thickness symptomatic grade three or four chondral defects larger than 2 cm^2.[4]

AMIC® for Cartilage Regeneration

Your Challenge

As an orthopedic surgeon today, you face a growing number of treatment challenges. Your patients are living longer, more active lives than previous generations. At the same time, obesity rates are rising. Active patients with cartilage damage expect a quick return to sports. Baby boomers want to stay active as long as possible, and avoid invasive surgical treatments.

With these changes in demographics, mindsets, and lifestyles, finding more regenerative treatment approaches for your patients will be critical in the coming years.

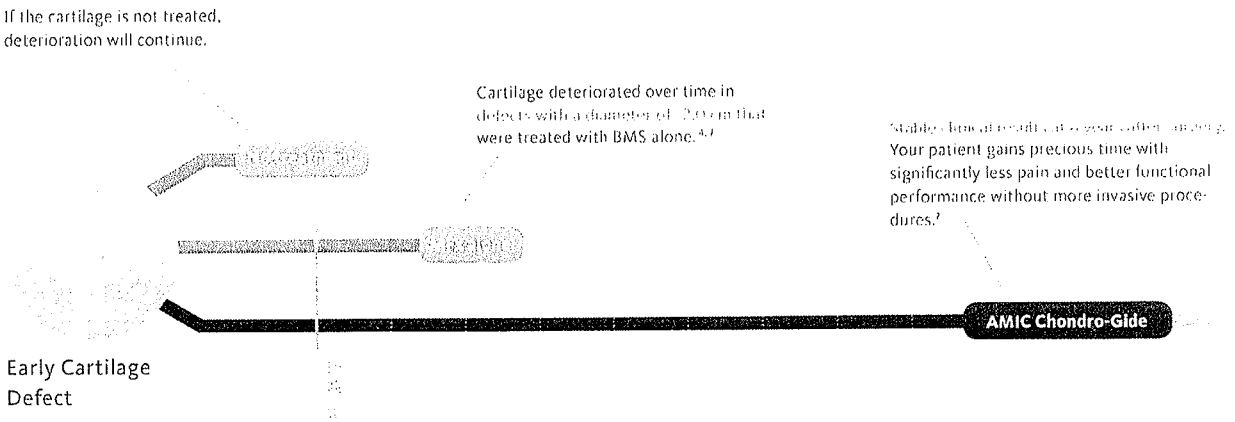
The Solution

Chondro-Gide®, a bio-derived collagen membrane, combined with Autologous Matrix-Induced Chondrogenesis (AMIC®) is a 1-step treatment for repairing cartilage lesions. Developed by Geistlich Surgery in collaboration with leading surgeons, AMIC uses bone marrow stimulation (BMS) in combination with Chondro-Gide to support the body's own healing potential.

Why Chondro-Gide

Backed by more than 10 years of clinical experience[5], AMIC Chondro-Gide is an effective and cost-effective technique[6] for repairing cartilage lesions, alleviating or preventing pain, and slowing the progression of damage.

FIGURE 1: REGENERATION OF CARTILAGE BUYS PRECIOUS TIME



Developed to Support Regeneration: Chondro-Gide®

Geistlich Surgery is a leader in the field of regenerative orthopedics, which leverages the body's own ability to repair bone and cartilage.

A Better Alternative to Standard MFx

MFx is commonly used in cartilage repair surgeries to recruit cells and other key bone marrow components to the site of the defect to support the regeneration of cartilage tissue. In larger lesions[8], the blood clot resulting from MFx is not stable enough to withstand shear forces in the joint.

AMIC® Chondro-Gide addresses this problem by combining BMS techniques with the use of a collagen membrane, which covers and protects not only the super clot but also the newly formed repair tissue.[9]

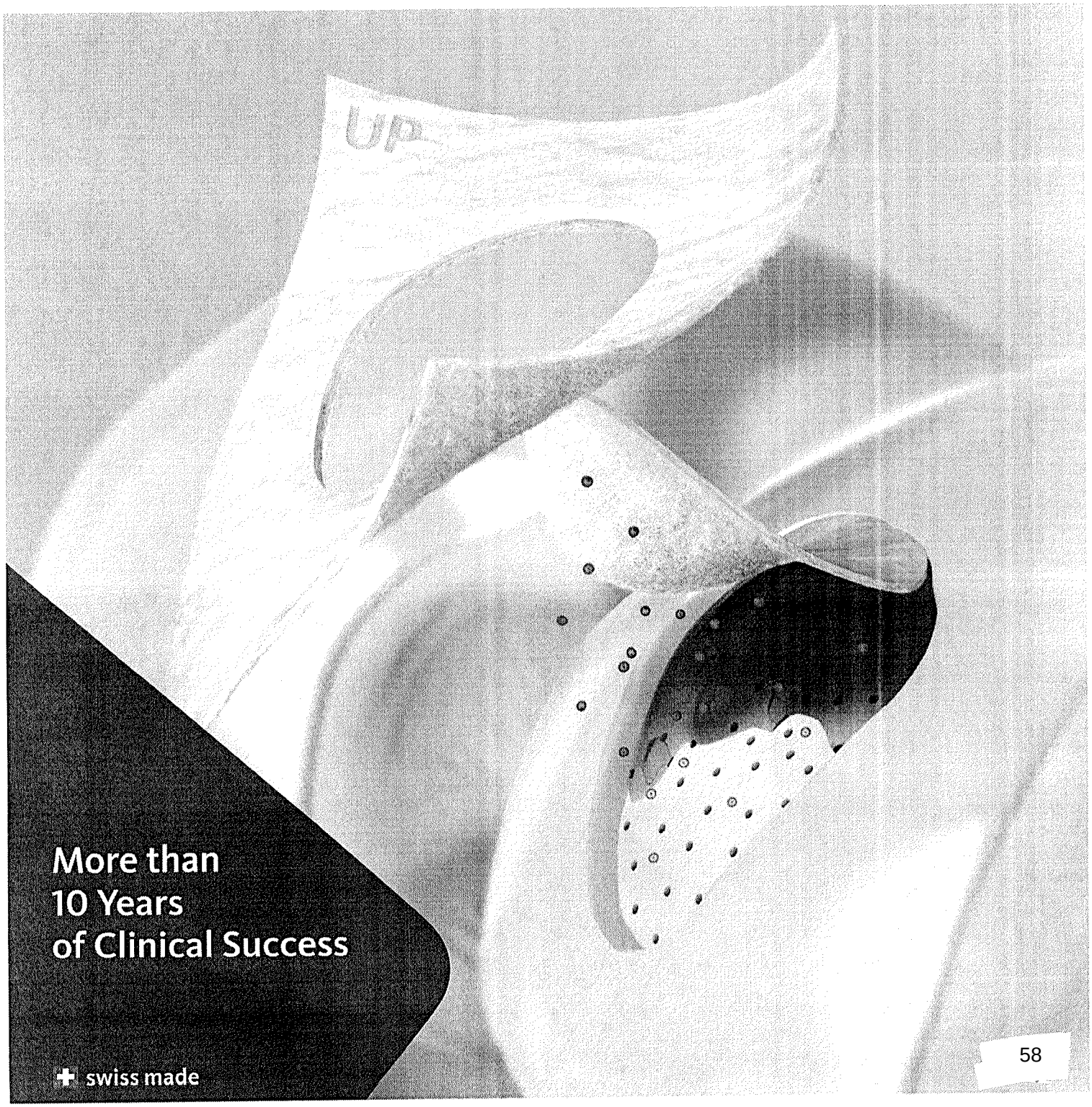
Chondro-Gide is a biocompatible and fully resorbable porcine collagen membrane. It was developed by Geistlich for use in AMIC Chondro-Gide, a minimally-invasive 1-step treatment to treat procedure to treat chondral lesions that is backed by more than 10 years of clinical experience.

Chondro-Gide Features[10]

- **Bio-derived, bilayer Collagen I/III membrane[10]**
- **Biocompatible and naturally resorbed[10]**
- **Easy to handle: supple and tear-resistant[10]**
- **Can be glued[10]**
- **Compatible with a range of tissue regeneration techniques[11]**
- **1-step procedure[10]**

Geistlich
Surgery

AMIC® Chondro-Gide® in the Knee



About Geistlich Surgery

Geistlich Surgery produces innovative bio-derived matrix products for bone and cartilage, including Orthoss®, Orthoss Collagen®, and Chondro-Gide®. Our products leverage the body's own healing potential to regenerate bone and cartilage. Our focus is on helping people maintain and regain their quality of life.

Geistlich Surgery is a business unit of Geistlich Pharma AG, which is headquartered in Switzerland. Entirely family owned since 1851, the company develops, produces, and markets medical devices for regenerative medicine and pharmaceuticals. From research and development to marketing, our operations are fully integrated under one roof, which enables us to oversee and optimize all levels of our business.

Geistlich and Collagen

Geistlich was among the first pharmaceutical companies to apply collagen for medical use in the 1990s. With more than 160 years experience with bio-derived bone and collagen products, we applied our extensive knowledge of collagen and its biofunctionality to develop the first collagen membrane to foster regeneration by providing a protective environment for the cells and nutrients that are essential for regrowth.

As experts in bone and tissue regeneration, we see tremendous potential for collagen in the future of regenerative medicine. That is why we have dedicated a team of biochemists, materials scientists, process engineers, and other experts at our headquarters in Switzerland to focus exclusively on collagen, and to explore its other possible therapeutic applications.

Through close relationships with the medical and scientific community, we continue to share our knowledge and optimize our collagen-derived products. Finding ways to improve peoples' quality of life remains our larger goal.

Several studies report articular defects in 60–66% of knees undergoing arthroscopy for pain. Of these, 55% were larger than 2 cm^2 in size.[1]

CONTENTS

AMIC® for Knee Cartilage Regeneration

Your Challenge

As an orthopedic surgeon today, you face a growing number of treatment challenges. Patients are now living longer and are more physically active than previous generations. While many are staying active as they age, some are overweight.

With these changes in longevity and lifestyle, patients are using the major joints of their bodies more than ever. As a result, the number of patients with knee cartilage damage is rising. But with developments in diagnostic arthroscopy and Magnetic Resonance Imaging (MRI), early and precise detection and treatment is now possible.

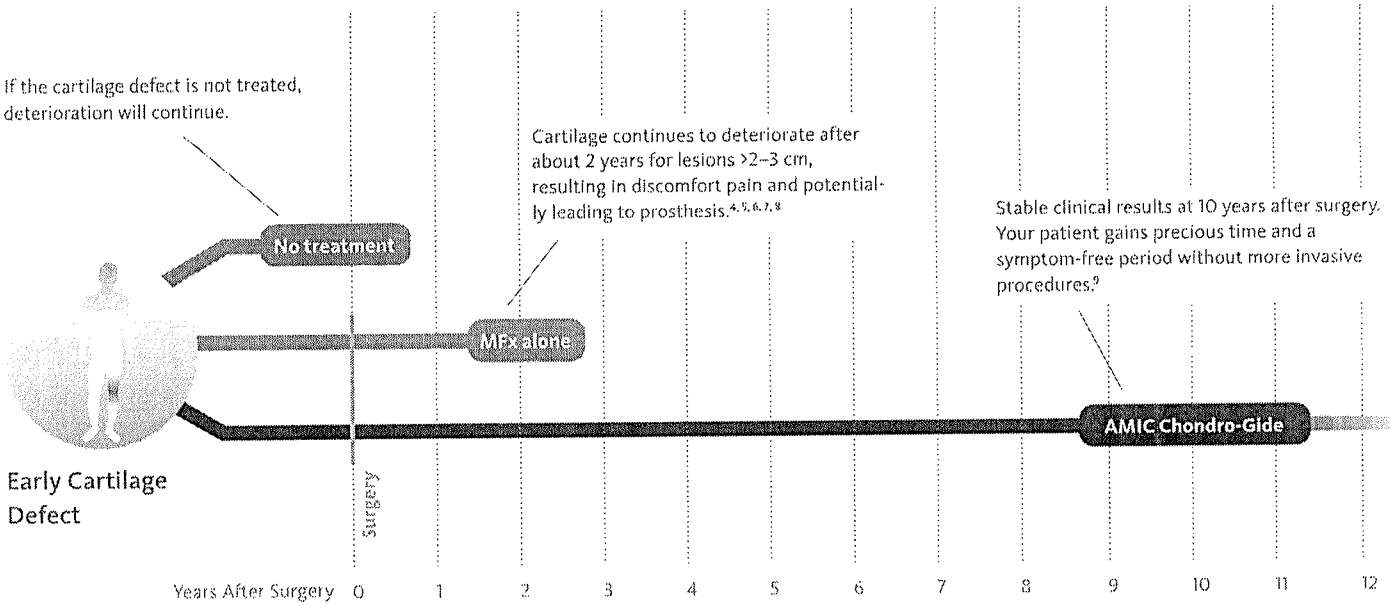
The Solution

Chondro-Gide®, a bio-derived collagen membrane, combined with Autologous Matrix-Induced Chondrogenesis (AMIC) is a 1-step treatment for repairing cartilage lesions. Developed by Geistlich Surgery in collaboration with leading surgeons, AMIC uses bone marrow stimulation (BMS) in combination with Chondro-Gide to support the body's own healing potential.

The Results

Backed by more than 10 years of clinical success, AMIC Chondro-Gide is an effective and cost-effective[2,3] treatment for repairing cartilage lesions, alleviating or preventing pain, and slowing the progression of damage.

REGENERATION OF CARTILAGE BUYS PRECIOUS TIME



Developed to Support Regeneration: Chondro-Gide® and AMIC®

Geistlich Pharma is a leader in the field of regenerative orthopedics, which leverages the body's own ability to repair bone and cartilage.

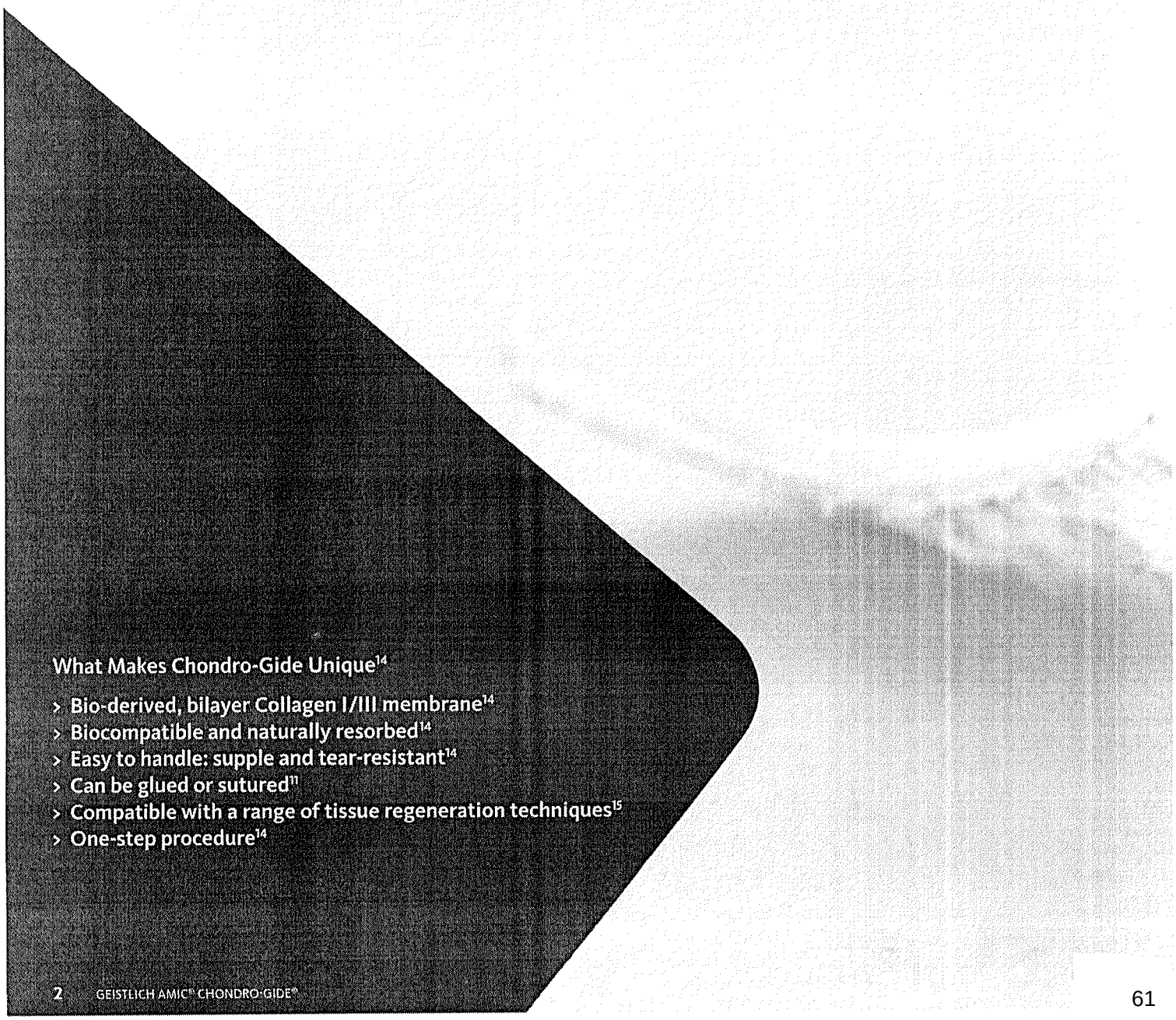
A Better Alternative to Standard MFx

Standard MFx is commonly used in cartilage repair surgeries to recruit mesenchymal stem cells and other key bone marrow components to the site of the defect to support the regeneration of cartilage tissue. In larger lesions[10], the blood clot resulting from MFx is not stable enough to withstand shear forces in the joint.

AMIC Chondro-Gide addresses this problem by combining standard MFx with the use of a collagen membrane, which covers and protects not only the super clot but also the repair tissue.[11] Chondro-Gide is a biocompatible and fully resorbable porcine collagen membrane developed by Geistlich for use in AMIC Chondro-Gide, a one-step procedure that is backed by more than 10 years of positive clinical results.[9]

Effective for Both Large and Small Defects

AMIC Chondro-Gide was developed specifically to treat cartilage lesions in articular joint surfaces. While standard MFx is generally recommended for small chondral defects (<2 cm^2), AMIC Chondro-Gide is an effective solution for larger defects.[6, 11, 12, 13]



What Makes Chondro-Gide Unique[14]

- Bio-derived, bilayer Collagen I/III membrane[14]
- Biocompatible and naturally resorbed[14]
- Easy to handle: supple and tear-resistant[14]
- Can be glued or sutured[11]
- Compatible with a range of tissue regeneration techniques[15]
- One-step procedure[14]

Bioengineered to Leverage the Body's Own Healing Potential

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. This provides a protective environment for the stabilization of tissue repair.[14,16]

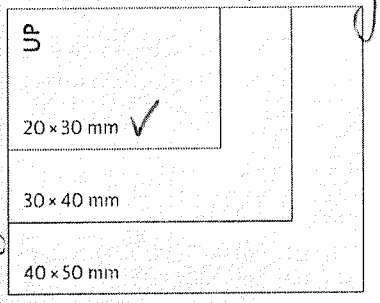
4.3 Chondro-Gide yra dvisluoksnė I/III tipo kolageno membrana, kuri yra lygi ir stipri, iš vienos pusės ir šiurkšti, akyta iš kitos. Tai suteikia apsauginę aplinką audinių atstatymo stabilizavimui.

Trys dydžiai

CHONDRO-GIDE IS AVAILABLE IN THREE SIZES

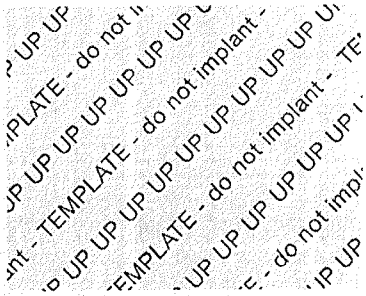
The top layer of the membrane is marked with the word "UP" in one corner.

4.5. Membranos dydis



A STERILE ALUMINUM TEMPLATE IS INCLUDED

The size and shape of the membrane patch can be determined with the sterile aluminum template.



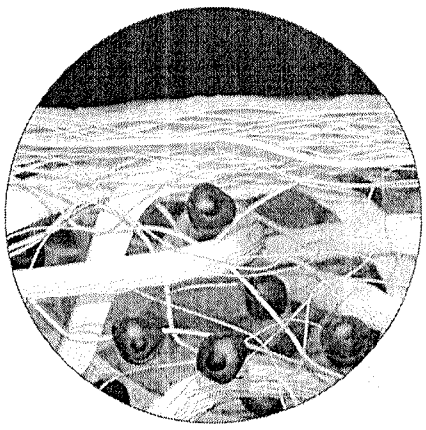
38 × 48 mm

Specialus aliumininio šablonas membranos pjaustymui pagal defekto dydį.

Barjeras, saugantis ląsteles difuziją. Lygus, stiprus viršutinis sluoksnis, patenkantis trintas, apsaugantis ląsteles ir naujai besiformuojančią kremzlę nuo trinties streso sąnaryje.

A Barrier to Prevent Cell Diffusion[14,17]

The smooth, compact top layer is also sturdy enough to protect the cells and newly forming cartilage from shear stress in the joint, while the cartilage regenerates and patients undergo rehabilitation.



Šiurkštus, akytas apatinis sluoksnis prilimpa prie defekto, laikydamas membraną vietoje. Ląstelės, kurios mikrofraktūros pagalba yra išlaisvintos iš kaulo, čiulpus stimuliuojančios technikos pagalba išlaisvintos ląstelės, prilimpa prie šio sluoksnio, kur jos dauginasi.

A Rough, Porous Bottom Layer

This layer adheres to the defect, keeping the membrane in place. Cells that are released through MFx or other marrow stimulation techniques attach themselves to this layer, where they proliferate and produce new tissue.[15,18]

AMIC®
Chondro-Gide®

AMIC Chondro-Gide is a minimally-invasive 1-step procedure that can be performed either by mini-open surgery, or in an arthroscopic manner.

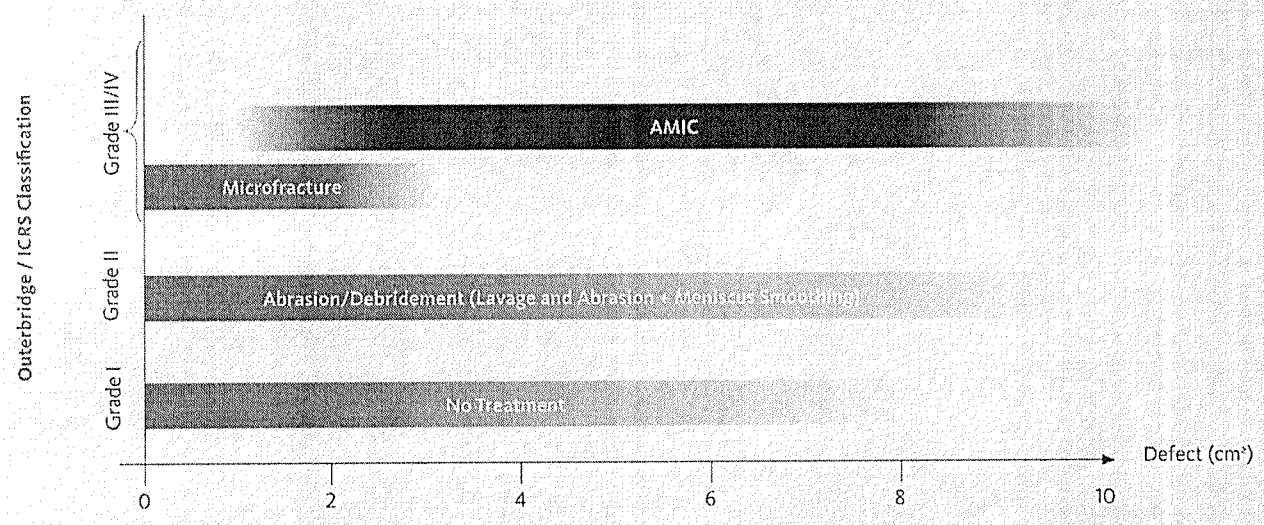
Developed by Geistlich Surgery in collaboration with leading surgeons in Europe, this technique has been effective in repairing chondral or osteochondral defects in the knee, talus, and hip.[3, 11, 12]

The Benefits of Using AMIC Chondro-Gide

With both mini-open and arthroscopic techniques, the unique advantage of AMIC Chondro-Gide is that it supports the body's own potential to heal itself. Damaged cartilage is removed, and then the subchondral bone is microfractured or drilled to release supply of fresh, viable mesenchymal stem cells.

The membrane covers the defect and serves as a protective shield that contains the cells and minimizes the impact of shear forces on the delicate superclot. At the same time, it functions as the roof of a biological chamber that forms over the defect. The biocompatible collagen material provides an environment for cell growth[14] and is replaced by new cartilage tissue over time.[16]

INDICATIONS FOR AMIC CHONDRO-GIDE



INTENDED USE[20]

Chondro-Gide® is used to cover cartilage defects treated with autologous chondrocyte implantation (ACI) or bone marrow stimulation techniques (e.g., AMIC® – Autologous Matrix Induced Chondrogenesis) and to cover meniscal or osteochondral defects. Surgical approaches include arthrotomy or arthroscopy. The defects can be acute or chronic and be caused by a fall, accident, or other traumatic events. Defects are located at articular cartilage surfaces including hyaline cartilage in the knee, hip, ankle foot, wrist, elbow, and shoulder; and fibrous cartilage including meniscus.

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LIMITATIONS ON USE / PRECAUTIONS

Contraindications

Chondro-Gide should not be used in patients with:

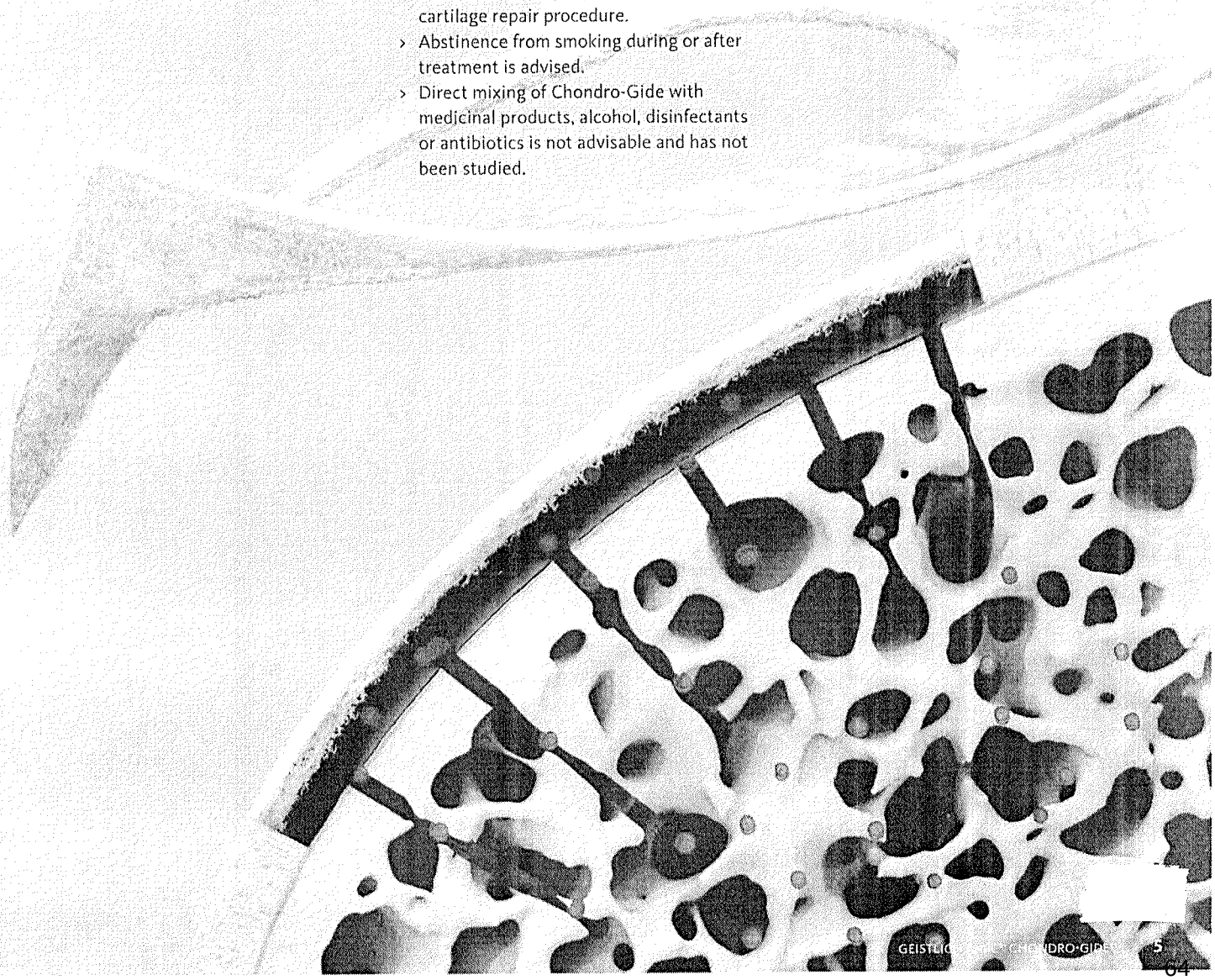
- a known allergy to porcine collagen
- acute or chronic infection at surgical site
- acute or chronic inflammatory joint disease.

Precautions

- Chondro-Gide should only be used by surgeons, familiar with cartilage and meniscal repair techniques.
- Chondro-Gide should be used with special caution in patients who take medications or have diseases impairing tissue regeneration.
- Chondro-Gide should be used only under standard sterile surgical conditions.
- Use of non-powdered gloves should be considered when preparing and handling Chondro-Gide to prevent transfer of particulate to the surgical site.
- Insufficient fixation of the membrane can lead to its displacement.
- Consistent with clinical practice of cartilage repair, any axial limb malalignment, joint instability or meniscal pathologies should be treated in parallel or prior to the cartilage repair procedure.
- Abstinence from smoking during or after treatment is advised.
- Direct mixing of Chondro-Gide with medicinal products, alcohol, disinfectants or antibiotics is not advisable and has not been studied.
- Intraoperatively, if there is need to remove the product, complete removal can be achieved. In the postoperative phase, complete removal may not be possible since the product is intended to resorb over time
- There is no data available on the use of Chondro-Gide during pregnancy or lactation. For safety reasons, pregnant women and breastfeeding mothers should therefore not be treated with Chondro-Gide.
- The safety and efficacy of Chondro-Gide have not been studied in children.
- The template must not be implanted.
- The product is intended for single patient, single surgery use, the product must not be re-sterilized. Any unused material should be discarded.

Side Effects

As Chondro-Gide is a collagen product, allergic reactions to collagen may not be totally excluded.



Bioengineered to Leverage the Body's Own Healing Potential

A Smooth, Compact Top Layer

A Barrier to Prevent Cell Diffusion

Flexible and Strong, to Protect New Cartilage

Safety and Quality

Enhanced Microfracturing and Chondro-Gide®: Effective and Cost-Effective

A Proven Track Record of Success for AMIC® with Chondro-Gide®

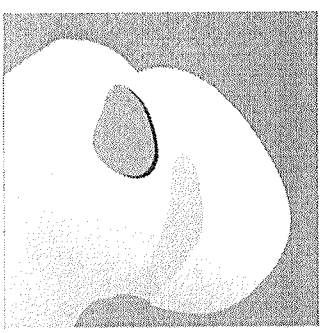
A Rough, Porous Bottom Layer

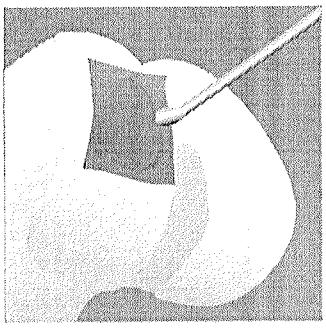
A Bio-Derived Collagen Membrane

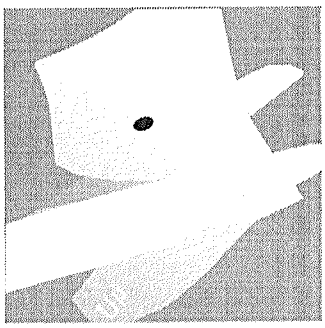
Ideal Conditions for Cell Attachment and Growth

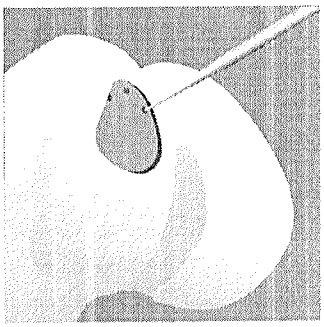
A Stable Environment for Regeneration

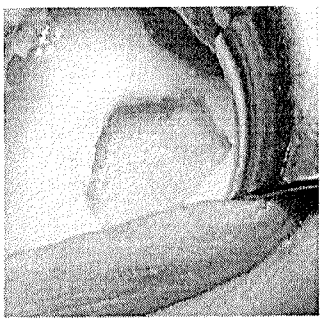
Mini-Open Surgery

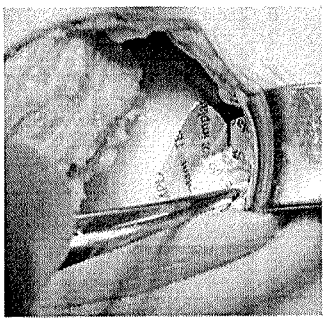


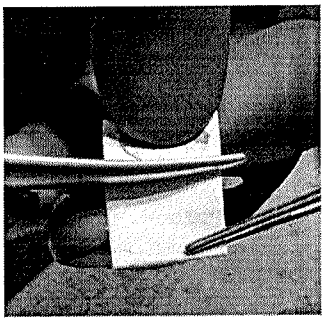












Prepare the Surgical Site

Using a standard, minimally invasive anterior approach, open the knee joint. Remove damaged and unstable cartilage with a scalpel, curette, and spoon until a stable, perpendicular shoulder surrounds the defect.

Measure the Defect

Place the sterile aluminum template included with the Chondro-Gide® in the defect to obtain an exact impression of the defect. Cut out the imprint and transfer it onto the membrane. The side that was facing the defect must be placed on the smooth layer of the Chondro-Gide.

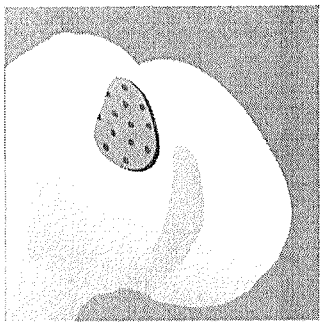
Trim the Chondro-Gide

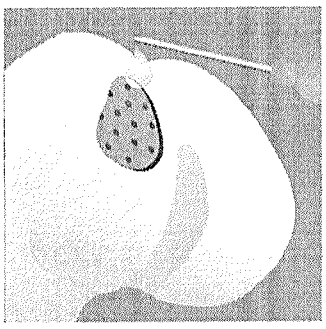
When trimming the Chondro-Gide, remember to cut it 10–15% smaller than the template, as the area of the Chondro-Gide will expand once moistened. Supple and soft when wet, the membrane can be easily positioned to conform to defects of various shapes. If needed, use a sterile pen to lightly mark the smooth (top) layer that will face the joint cavity. The "UP" sign might not be visible any more once you have cut or hydrated the membrane.

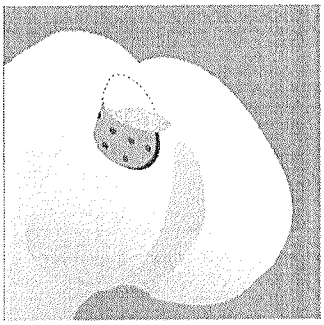
Perforate the Bone

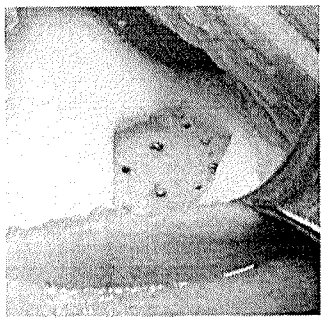
Use a sharp awl or drill to perforate the subchondral bone at the base of the lesion. Start at the periphery of the lesion and then move toward the center at intervals of 3–4 mm[21]. With adequate cooling, antegrade drilling is also possible.

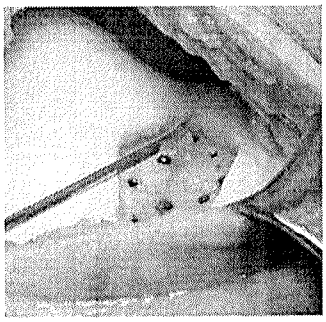
▶ Prior to surgery during diagnostic arthroscopy, carefully assess the size and classification of the defect. If necessary, carry out concomitant interventions, e.g., meniscal repair, alignment or stabilization.

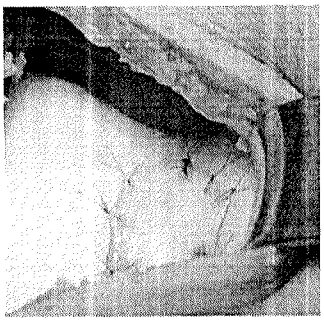












Remove the Residual Tissue

Carefully remove the residual tissue and check for adequate subchondral bleeding.

Secure the Chondro-Gide®

Apply fibrin glue directly to the subchondral bone plate around the perforations.

Position and Glue the Chondro-Gide®

Place the Chondro-Gide into the defect with the rough (bottom) layer facing the bone surface.

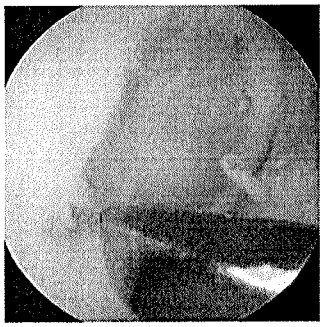
Check the position of the membrane and close. Once the glue has set, after about 5 minutes, use a sharp scalpel to remove the excess fibrin glue carefully. To prevent delamination of the membrane, make sure the Chondro-Gide is flush with the edge of the defect.

Suturing Instead of Gluing

Using a TF-plus needle (inside-out technique, single stitches every 5 mm), attaching the Chondro-Gide with Vicryl or PDS 6/0 sutures is also possible.

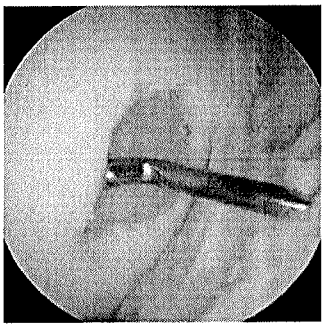
▶ Check to make sure the membrane is positioned properly and stable by bending and extending the knee 10 times. To complete the surgery, carefully stop the bleeding, and suture the wound. If applying a drain, use a non-suction drain.

Arthroscopic Surgery



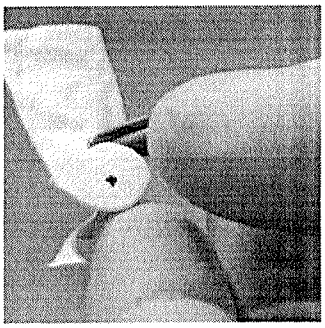
Prepare the Surgical Site

Use a sharp curette to remove cartilage fragments and create smooth vertical defect walls.



Measure the Defect Size

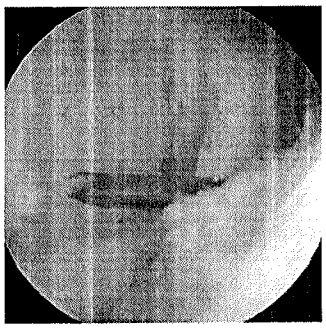
Using a probe, measure the defect size. Turn the probe in different directions to determine the diameter and shape of the defect. Transfer the measurement in the same way onto the Chondro-Gide®.



Prepare the Chondro-Gide

Once the Chondro-Gide has been cut, moistened and is inside the joint, distinguishing the smooth from the rough layer might be difficult. Use a sterile pen to lightly mark the smooth (top) layer of the Chondro-Gide that will face the joint cavity.

When trimming the Chondro-Gide, remember to cut it 10–15% smaller than the defect itself, as the area of the Chondro-Gide will expand once moistened.



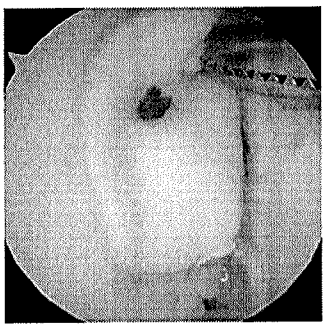
Microfracturing

Using a 1.2 mm K-wire, perforate the subchondral bone at the base of the lesion. Working from the periphery of the lesion towards the center, insert holes at intervals of 3–4 mm. With a shaver, carefully remove tissue fragments. Alternatively, you can use an awl or nanofracturing to perforate the subchondral bone.

▶ Prior to surgery during diagnostic arthroscopy, carefully assess the size and classification of the defect. If necessary, carry out concomitant interventions, e.g., meniscal repair, alignment or stabilization.

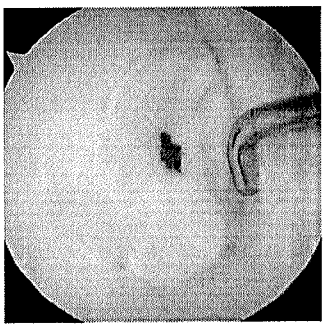
Position the Chondro-Gide®

Use forceps or a clamp to place the membrane in the defect. To prevent delamination of the membrane, make sure the Chondro-Gide is sitting flush inside the defect.



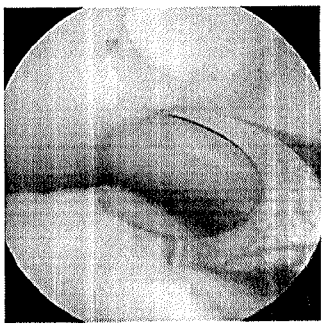
Apply the Glue

Inject fibrin glue into the space between the Chondro-Gide and the defect. Apply the glue at the top of the lesion and then let it flow to the lower part.



Secure the Chondro-Gide

Using an arthroscopic probe, tap the membrane into place.



Remove the Excess Glue

With a probe or a shaver, remove the excess fibrin glue.

NOTE

In addition to the wet arthroscopic technique illustrated above[22], AMIC® can also be performed using a dry approach. The successful use of the dry technique has been described by different surgeons.[23, 24] Choose wet or dry AMIC as you prefer.

▶ Check to make sure the membrane is positioned properly and stable by bending and extending the knee 10 times. To complete the surgery, carefully stop the bleeding, and suture the wound. If applying a drain, use a non-suction drain.

Clinical Summaries

Consistently Positive Results at 10 Years

Mini-Open Surgery

A 10-year follow-up study by Kaiser et al.[9] investigated the use of AMIC® in the treatment of chondral and osteochondral defects in the knee. Average Lysholm Scores and Visual Analogue Scores (VAS) for pain improved significantly when the pre-operative values were compared to the results at 2- and 10-year post-operative. Importantly, the improvement of these key scores was maintained over the 2 to 10-year follow up. This study demonstrated that AMIC offers significant improvement over the pre-operative status as well as long-term durability of results.

AMIC Shows Better Performance Than MFx Alone After 5 Years in a randomized, controlled study

In a multi-center, randomized, controlled 3-arm study by Volz et al. a significant deterioration in results was seen after 2 years when the treatment was MFx alone without Chondro-Gide®.[11]

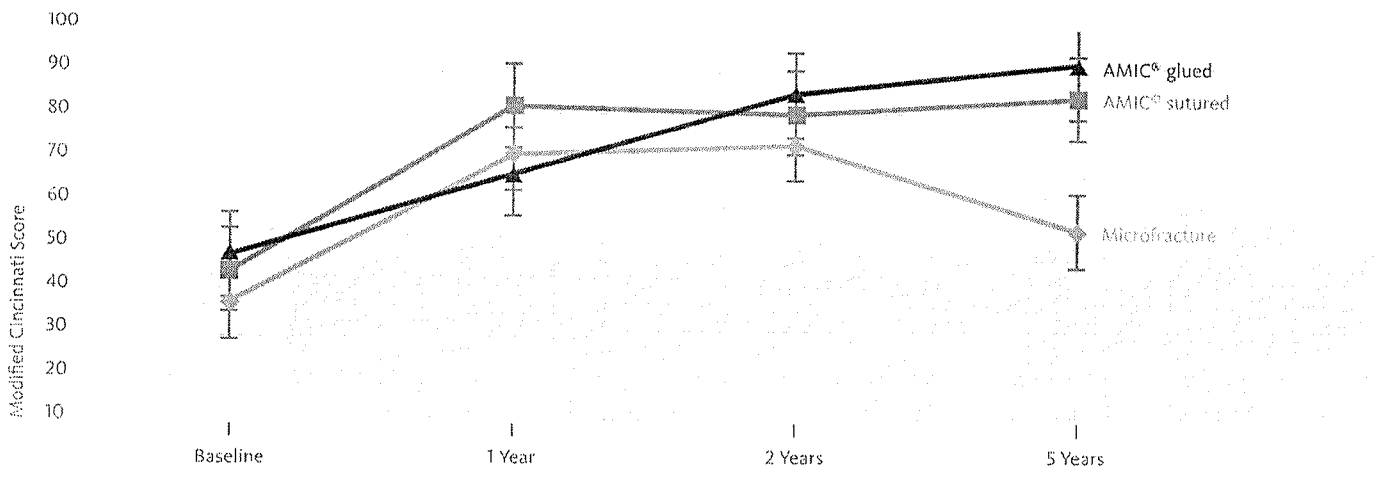
All treatment groups in the 3-arm study showed significant improvement in the first year, followed by stabilization at 2 years. However, at 5 years, results of the AMIC Chondro-Gide patients were different from those of the MFx-only patients. Pain and function scores (ICRS and modified Cincinnati scores) remained stable or even improved with AMIC, while pain and function scores for the MFx group decreased after 2 years (figure 1).

Overall, the results of this study are consistent with the observations from other published studies that show positive mid-to long-term clinical results for AMIC, while clinical outcomes for patients treated with MFx alone show a decline in performance after 2 years.[4,5,25,26]

First meta-analysis of 12 AMIC Chondro-Gide studies including 375 patients with a mean defect size of over 4 cm^2 demonstrates significant and sustainable improvement of knee function and pain[13]

Most recently, (2019) in a systematic review and meta-analysis of AMIC outcomes, the authors evaluated grade III/IV chondral and osteochondral lesions in the knee with a mean defect size of 4.24 cm^2. The meta-analysis included 12 studies and compared VAS, Lysholm and IKDC scores between baseline and follow-up after 1 or 2 and more than 3 years. It demonstrated that the use of AMIC Chondro-Gide in defect sizes, which are above the recommended threshold for MFx, significantly reduced pain and improved function from baseline to follow-up. The clinical outcomes suggested that AMIC provides a clinical benefit for at least 5 years, some of the studies even show stable results after 7 years. This publication is the first me-

FIGURE 1: FUNCTIONAL STATUS OVER TIME[11]



ta-analysis of a one-step cartilage repair technique with only one scaffold used (Chondro-Gide®).[13]

Significant and sustainable improvement of knee function and reduction of pain at 7 years

A retrospective analysis by Schiavone Panni et al.[2] noted that AMIC® was effective when treating full-thickness knee cartilage defects larger than 2 cm^2. Over an average 7-year follow-up, patients consistently showed significant clinical and functional improvement based on their International Knee Documentation Committee (IKDC), MRI, and Lysholm scores.

ACI-C and AMIC Chondro-Gide provide equally good results after 2 years

Most recently, Fossum, et al., (2019) conducted a prospective, randomized, controlled study to assess the outcomes of ACI-C and AMIC in chondral and osteochondral defects of the distal femur and patella. At 1 and 2 years, the mean function and pain scores were compared with baseline scores and showed significant improvement. No significant differences were seen between the outcomes of the ACI-C and AMIC techniques. The authors concluded that AMIC could be considered a clinically equal, but less expensive alternative to ACI-C, as AMIC is a 1-step procedure therefore far less resource-intensive.[27]

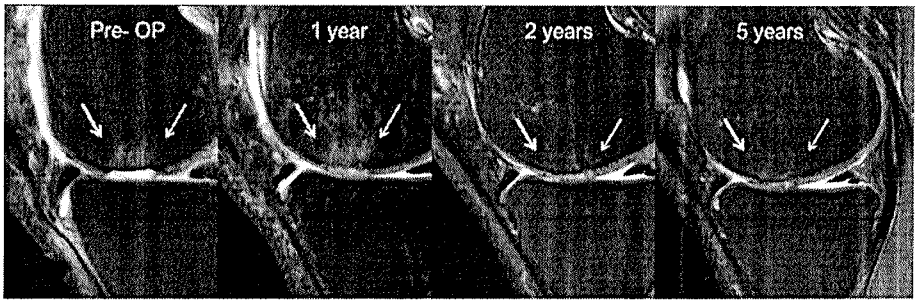
Arthroscopic Surgery

Arthroscopic Technique Equally Positive as Mini-Arthrotomy with AMIC Chondro-Gide

In a retrospective study, Schagemann et al.[22] compared the clinical outcomes of AMIC Chondro-Gide procedures that were performed as either arthroscopic or mini-open surgeries. The study followed patients for 2 years.

According to the patients' Visual Analog Scale (VAS) pain scores, Lysholm scores, and Knee injury and Osteoarthrithis Outcome Scores (KOOS), both surgical approaches yielded equally positive results.

FIGURE 2: CARTILAGE DEFECT REPAIR AFTER AMIC®



MRI (1.5T) follow-up at 1,2, and 5 years after AMIC® shows progressive defect filling (20 × 20 mm, see arrows).[11] Image from Volz et al. CC BY 4.0

Reparing Patellar Cartilage Lesions with AMIC Chondro-Gide

In another 2017 study, Sadlik et. al.[24] analyzed 12 patients who had undergone arthroscopic surgery using AMIC Chondro-Gide to repair patellar cartilage lesions. The Sadlik study assessed patients before surgery and at an average follow-up time of 38 months. Both clinical and radiological results improved significantly, according to criteria including KOOS, International Knee Documentation Committee (IKDC), Visual Analog Scale (VAS), Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scores, and MRI.

Using augmented MFx in combination with Chondro-Gide, both arthroscopic and mini-open have been shown to be successful treatments for more than 10 years. Using augmented MFx with Chondro-Gide makes this technique even more effective, with enhanced healing and stability.

Beyond Microfracture

Designed to be used in combination with MFx and Autologous Chondrocyte Implantation (ACI), Chondro-Gide is equally well-suited to be used with other bone marrow stimulation techniques.[28,29] The unique bilayer structure of the membrane is key. With a porous and a cell-occlusive layer, Chondro-Gide acts as both a cover or wrapper that encloses cell-rich material while also providing a protected environment for regeneration.

A review by Lee et al.[30] on AMIC and related techniques in the knee also documents the trend to add concentrated bone marrow-derived mesenchymal stem cells (MSCs) and Platelet-rich plasma, alone or in combination.

Bone marrow has been shown to be a possible source of multipotent stem cells with chondrogenic potential and can be harvested during the same surgical procedure. Gobbi et al.[31] used bone marrow-derived MSCs and Chondro-Gide for large full-thickness chondral lesions of the knee. They demonstrated lasting post-operative results up to 3 years.

Another approach, presently in Phase II, uses nasal chondrocytes. They can be easily accessed and demonstrated their capacity to support articulate cartilage repair.[17] Cells from a nose biopsy are seeded and expanded on the Chondro-Gide, the structure of which is perfect for this tissue culture approach. It allows a simple loading of the cells on the rough layer, while the smooth cell occlusive layer keeps the cells in place. The cultured tissue is then sutured into the cartilage lesion site. First clinical results showed statistically significant improvements in all categories.[17]

Rehabilitation and Follow-Up Treatment

Within a few days after surgery, patients can begin partial weight-bearing, supporting a small amount of weight (up to 50%) using the operated leg. However, they should not try full weight-bearing for approximately 6 weeks. Patients should take a gradual approach to increasing activity, but by 6 months after surgery, most should be able to resume their regular sports activities.

Key factors in determining whether a patient has recovered and can return to sports activities are whether the patient's state of healing has been accurately assessed, and whether the patient is ready to resume an active lifestyle.

As objective and subjective measures of healing often yield contradictory results, using both presents challenges in managing patient expectations.

In 2016, researchers correlated the results of subjective assessments, such as International Knee Documentation Committee (IKDC) and Lysholm scores, with objective isokinetic tests in patients who had undergone arthroscopic AMIC® in the knee. The results showed that while both objective and subjective measures were useful in monitoring a patient's overall rehabilitation progress, the IDKC and Lysholm tests were particularly useful in determining a patient's general state of recovery and readiness to return to sports activities.[32]

Postoperative Rehabilitation after Cartilage Repair in the Knee

Stationary Phase

- Prior to first mobilization, position the knee post-op in full extension in a splint and foam splint.
- Mobilization on the first day by a physiotherapist
- CPM/Kinetec: start with 30°/0/0 for ca. 2 hours/day (restricted by pain)

General (Depending on Availability)

- Individual therapy during the first 12 weeks
- Lymphatic drainage as needed to reduce excessive swelling
- Hydrotherapy starting from week 6
- Targeted medical training, including gait training from week 8

Active, Weight-Bearing

- W 0–2 sole contact using crutches
- W 3–4 partial weight bearing on crutches 10–15 kg
- W 5–6 partial weight bearing on crutches 10–15 kg
- W 6–7 transition to full weight bearing

(Femoro-patellar) Gentle Treatment with Corresponding Angles for the First 6 Months

- Extension in open chain: 90°–40°; full flexion in open chain
- From W 8: squat/3 flex 0°–40°
- From W 12: leg press 0°–60°

Passive Mobilization

- W 0–1 ROM 30°/0/0
- W 2–3 ROM 60°/0/0
- W 3–4 ROM 90°/0/0
- W 5–6 ROM 120°/0/0
- CPM/Kinetec at home for ca. 3 hrs/d
- Bicycle ergometer without resistance (max. 90°) from week 6 on: increase progressively from week 8 on (restricted by pain)

Muscle Build Up/Proprioception/Coordination

- Optimize quadriceps innervation immediately
- Increase of load bearing mainly in closed kinetic chain
- Increase progressively from W 8 on (below pain threshold)

Active Mobilization

- W 0–2 ROM 30°/0/0
- W 3–4 ROM 60°/0/0
- W 5–6 ROM 90°/0/0

Bandage/Orthesis

- First 4–6 weeks in order to ensure limitation of movement, thereafter progressive reduction

Sports

- M 2 post-op walking on soft surface
- M 2 post-op cycling
- M 6 post-op jogging
- M 6 post-op mountain biking

W = week, ROM = range of motion, M = month, hrs/d = hours per day
Note: This is only an example of a plan that was developed by an orthopedic surgeon (M. Steinwachs, Sport Clinic, Zürich, 2018).[33,34] There is no agreement on one standardized algorithm in literature or among orthopedic societies.[19]

Geistlich Chondro-Gide®

Regulatory approvals for Geistlich Chondro-Gide vary by country.

To learn more about product availability please visit www.geistlich-surgery.com or contact the Geistlich distributor in your region.

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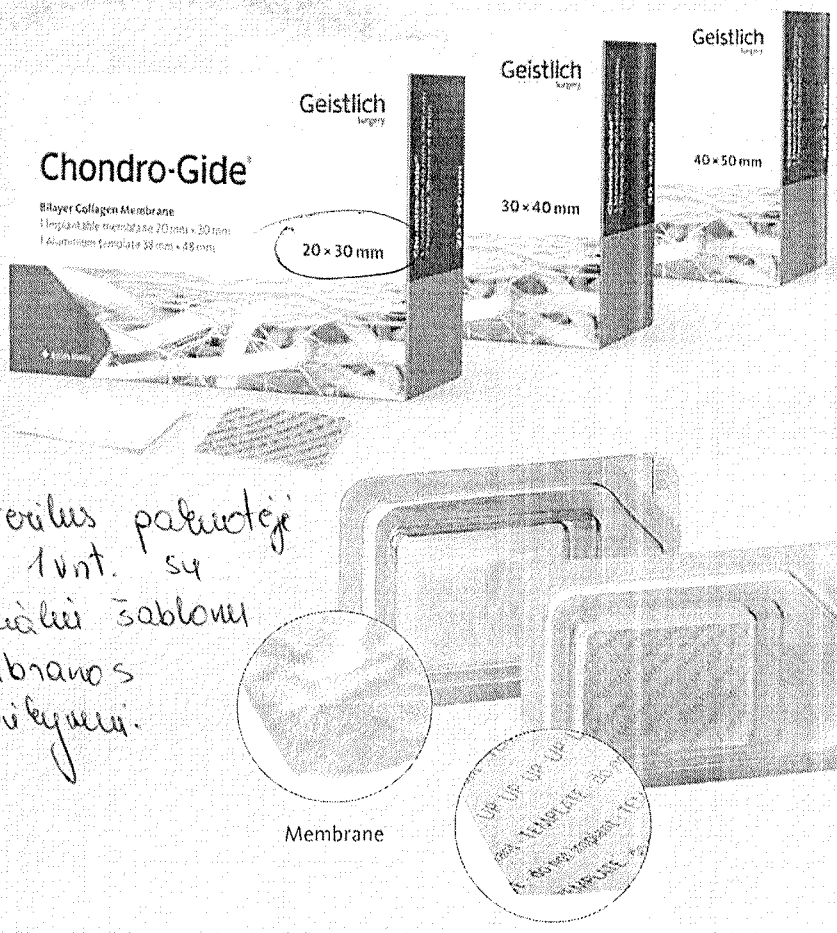

Sterilus pakuotėje po 1 vnt. su specialiu šablonu membranos pritaikymui.

Membrane

Template, do not implant

1 HJELLE, K., et al. Articular cartilage defects in 1,000 knee arthroscopies. Arthroscopy. Sep 2002, 18(7), 730-734. (Clinical study)

2 SCHIAVONE PANNI, A., et al. Good clinical results with autologous matrix-induced chondrogenesis (Amic) technique in large knee chondral defects. Knee Surg Sports Traumatol Arthrosc, 2018 Apr 26(4):1130-36 (Clinical study)

3 WALTHER, M., et al. Scaffold based reconstruction of focal full thickness talar cartilage defects. Clinical Research on Foot & Ankle, 2013, 1-5. (Clinical study)

4 MITHOEFER, K., et al. The microfracture technique for the treatment of articular cartilage lesions in the knee. A prospective cohort study. J Bone Joint Surg Am. Sep 2005, 87(9), 1911-1920. (Clinical study)

5 GOYAL, D., et al. Evidence-based status of microfracture technique: a systematic review of level I and II studies. Arthroscopy. Sep 2013, 29(9), 1579-1588. (Review of clinical studies)

6 FONTANA, A., et al. Sustained five-year benefit of autologous matrix-induced chondrogenesis for femoral acetabular impingement-induced chondral lesions compared with microfracture treatment. Bone Joint J, May 2015, 97-B(5), 628-635. (Clinical study)

7 GAO, L., et al. Early loss of subchondral bone following microfracture is counteracted by bone marrow aspirate in a translational model of osteochondral repair. Nature Scientific Reports, 2017, 7:45189. (Pre-clinical study)

8 FRANK, R.M., et al., Failure of Bone Marrow Stimulation Techniques. Sports Med Arthrosc Rev. 2017, 25 (1) (Review of clinical studies)

9 KAISER, N., et al. Clinical results 10 years after AMIC in the knee. Swiss Med Wkly, 2015, 145 (Suppl 210), 43S. (Clinical study)

10 MITHOEFER, K., et al. Clinical Efficacy of the Microfracture Technique for Articular Cartilage Repair In the Knee. An Evidence-Based Systematic Analysis. AJSM, 2009. (Review of clinical studies)

11 VOLZ, M., et al. A randomized controlled trial demonstrating sustained benefit of Autologous Matrix-Induced Chondrogenesis over microfracture at five years. Int Orthop, Apr 2017, 41(4), 797-804. (Clinical study)

12 JANNELLI E , et al. Arthroscopic treatment of chondral defects in the hip: AMIC®, MACI, microfragmented adipose tissue transplantation (MATT) and other options. SICOT J, 2017,3(43). (Clinical study)

13 STEINWACHS, M.R.,et al. Systematic Review and Meta-Analysis of the Clinical Evidence on the Use of Autologous Matrix-Induced Chondrogenesis in the Knee. Cartilage. 2019:1947603519870846. https://www.ncbi.nlm.nih.gov/pubmed/31508990 (Review of clinical studies)

14 Geistlich Pharma AG data on file (Bench test)

15 KRAMER, J., et al. In vivo matrix-guided human mesenchymal stem cells. Cell Mol Life Sci, Mar 2006, 63(5), 616-626. (Clinical study)

16 GILLE, J., et al. Cell-Laden and Cell-Free Matrix-Induced-Chondrogenesis versus Microfracture for the Treatment of Articular Cartilage Defects: A Histological and Biomechanical Study in Sheep. Cartilage OnlineFirst, January 7, 2010, doi:10.1177/1947603509358721 (Pre-clinical study)

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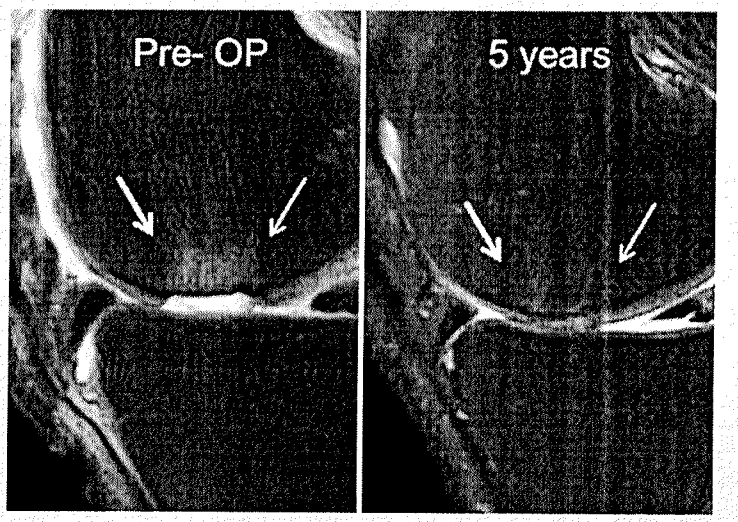

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To start using AMIC® Chondro-Gide® to alleviate or prevent patient pain and slow the progression of damage, contact your local Geistlich representative.

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4.6.

Komplette zu fibrinklebern Elspan

Baxter

United States

TISSEEL [Fibrin Sealant] Kit (Freeze Dried) with DUPLOJECT System - 2 mL

For Topical Use Only

SKU: 1504514

Provides all components for reconstitution and delivery of fibrin sealant. Each TISSEEL [Fibrin Sealant] Kit with DUPLOJECT System contains 1 DUPLOJECT applicator, 2 joining pieces, 4 application cannula tips, 4 syringes, 4 needles, and the TISSEEL package insert. Topical Use Only - Do Not Inject. Available in 3 sizes. Single use. Sterile and non-pyrogenic.

Grösse zu membranen Elspan

Product Characteristics

Latex:	Not Made with Natural Rubber Latex
Concentration:	Rx Only
Package Insert Link:	baxterpi.com/pi-pdf/Tisse(..)

Carton

Pack Factor:	1

Website Links

	www.tisseel.com
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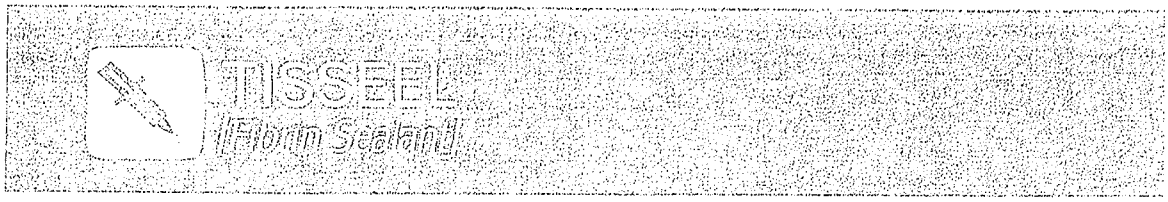
Ordering information

Baxter Product Code:	1504514
UPN/GTIN CS Unit:	60309444301028
UPN/GTIN EA Unit:	00303384301023
National Drug Code:	0944430102
Unit of Measure:	Each



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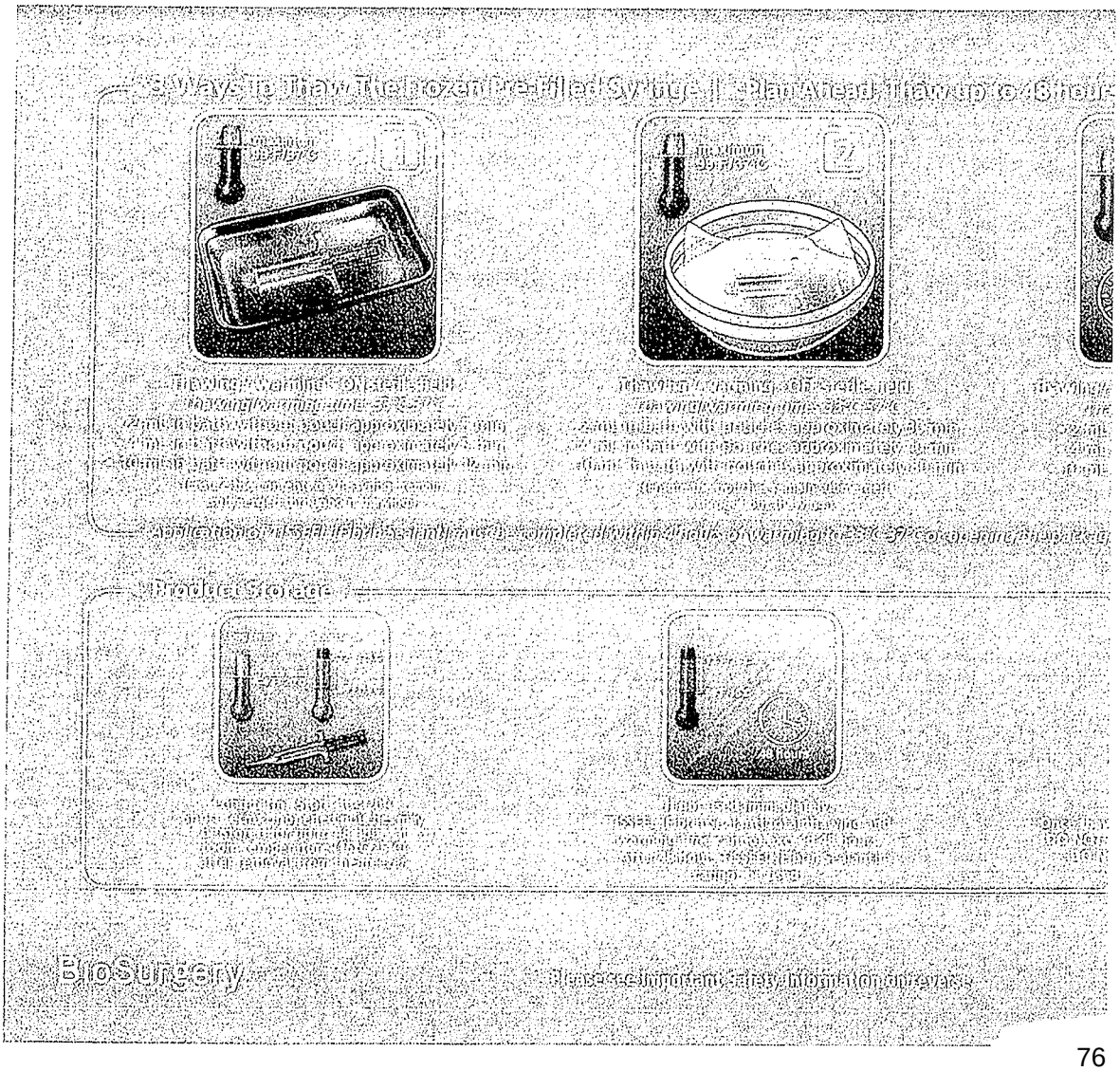

unilaki dvisluoksinė Chondro-Gide membranos struktūra

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