ChondroFiller liquid

Surgical technique

Introduction

There are a variety of methods for the treatment of articular cartilage defects to choose from. These procedures have very different advantages and disadvantages.
The autologous chondrocyte implantation (ACI) is the Gold Standard at the moment for articular cartilage treatment. It was first adopted in 1987 by Brittberg et al. In this first generation of ACI, the cartilage defect was covered with a periosteal flap. However, this technique had several disadvantages such as the periosteal hypertrophy, the loss of cells, the complexity of the surgical technique and the associated high revision rate. Therefore in the second generation carrier substances were designed which should solve the above mentioned problems. In this approach, the cells were placed in a 3-dimensional matrix, and then transplanted. The most widespread matrices where collagen-based. This kind of ACI was called matrix induced autologous chondrocyte implantation (MACI).

Despite the promising clinical results of the ACI/MACI, the serious disadvantage of this method is that it must be done in two steps: first a cartilage biopsy has to be done to recover the cells and in another surgery, the cultured cells with the support matrix have to be inserted into the defect. These methods are timeconsuming and involve high costs.
Therefore, there have been increasing efforts to develop a cartilage repair treatment with a cell-free and one-stage process in recent years.

A new approach is the use of a collagen gel which is already well established as a cell-based method (Andereya et al. 2006, Schneider et al. 2011). Further animal studies proved that the cell migrates into the collagen gel and differentiates into cartilage-like cells over time (Gavenis et al. 2010).
This results in a perfectly integrated and well differentiated cartilage tissue that comes very close to an embryonic cartilage tissue (Schneider et al 2011). First clinical applications of this cell-free matrix showed very good clinical and MRI results in the treatment of smaller local cartilage defects (Efe et al. 2012).
This technique, however, has the disadvantage of needing an arthrotomy of the joint in order to insert the cell-free implant. Through a modification in the production of this cell-free collagen gel, a purely arthroscopic application is now possible for the first time. This has the advantage of less trauma and rapid rehabilitation.

What is ChondroFiller^{liquid} ?

ChondroFiller^{liquid} is a ready to use two chamber syringe filled with components to create an autoregenerative collagen implant for the treatment of traumatic or degenerative articular cartilage defects. The applicable liquid implant matrix changes its state into a dimensionally stable, gel-like consistency within a short period of time. ChondroFiller^{liquid} allows the purely arthroscopic application of the implant matrix into the prepared cartilage defect without further opening of the joint. Because of this regions can be reached, which are usually impossible or very difficult to get to (posterior tibia plateau, retropatellar defects, ankle joint etc.). The chambers are filled with a neutralization solution and pure, native collagen type I which is isolated from rat tail tendons. The collagen type I content is 8 mg/mL, the total volume approx. 2.3 mL.

Indications/Contraindications

Indications

As with every new process, it is important to follow the indications and to consider contraindications. The following basic requirements should be met to ensure the successful application of the ChondroFiller^{liquid} technique:

- Preserved cartilage shoulder
- Intact surrounding cartilage
- Intact corresponding articular surface (damage to the corresponding surface up to an Outerbridge classification of grade II is permitted)
- Intact meniscus (a partial resection of up to max 1/3 of the total volume is permitted)
- Intact ligaments, physiological leg axis
- Free joint mobility
- Patients aged > 18 years
- Outerbridge classification: grade III and IV
- Defect size < 3 cm^2

Contraindications

In the presence of the following exclusion criteria the ChondroFiller^{liquid} technique should not be applied:

- Hypersensitivity and/or allergy to collagen or rat protein
- Multi-compartmental arthrosis
- Hematopoetic disorders
- Malignant disorders
- Neurological diseases
- Increased risk of bleeding
- Pregnant or breast feeding women
- Incapacitated and compulsory treatment patients
- Patients with a cartilage defect sized ≥ 2,5 cm in diameter
- Joint stiffness
- Arthrofibrosis
- Joint infections
- Metabolic diseases
- Leg malalignment of > 5°

Surgical technique ChondroFiller^{liquid}

Bearing

The bearing of the limb to be operated depends on the localization of the defect zone. If for example the defect is located in the main load region of the femoral condyle, it can be first debrided in the standard position. For the insertion of ChondroFiller^{liquid} the limb however must be bedded in such a way that the defect is localized nearly horizontal at the highest point to prevent drainage of the primary liquid gel. In retropatellar defects the patient must be placed in the face-down position. This should be clarified with the anaesthesiologist in advance.

Arthroscopy

In the first step, the arthroscopy of the joint takes place in standard technique. As part of the arthroscopy the indication for using ChondroFiller^{liquid} needs to be checked. Only if all indication criteria are met should this method be applied. Accompanying joint pathologies such as meniscal damage, ligament insufficiency, false position of the leg axis etc. should be treated first in the same session.
Alternatively the arthroscopy can be carried out with CO_2. This has the advantage of the cartilage defect being much better accessible which is not possible with conventional irrigation fluid-based arthroscopy.

Debridement of the defect

The debridement of the cartilage defect can be done after a mini arthrotomy either with a sharp spoon or with appropriately sized curettes. It is important that all diseased components are removed and a stable cartilage shoulder remains on all sides (Fig. 1). During the preparation of defect it is important to ensure that the subchondral plate is not broken. It has paid off to undermine the cartilage edges with appropriate instruments so that a good anchoring of the implant in the defect can be achieved. For a good documentation the debrided defect should be measured accurately. The preparation of ChondroFiller^{liquid} should take placeat the same time as the debridement (see preparation and application of ChondroFiller^{liquid}).

Arthroscopy with irrigation fluid

Arthroscopy with gas (CO_2)

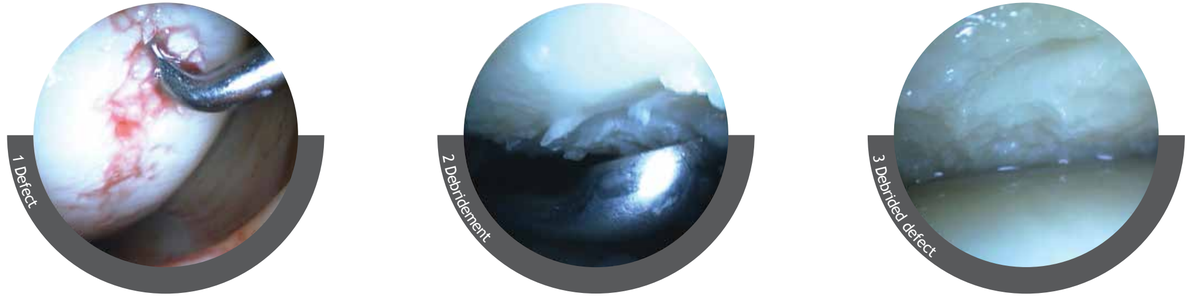


Fig. 1 Defect and debridement

Surgical technique ChondroFiller^{liquid}

Rearrangement before injection of ChondroFiller^{liquid}

Before injecting ChondroFiller^{liquid} the affected limb must be positioned in a way that prevents the primary liquid collagen from draining at the sides. Thus the bearing is highly dependent on the location of the defect. In femoral defects it is usually enough to fix the leg at 90° of hip and knee flexion. Defects of the trochlea and the tibia usually require no special bedding positions. Retropatellar defects usually have to be treated in the face-down position.

Drying of the defect prior application of ChondroFiller^{liquid}

Before applying ChondroFiller^{liquid} the cartilage defect area should be as dry as possible. When using irrigation fluid for arthroscopy it should be completely drained. The cartilage area should then be dried separately. The aspiration of the fluid with an aspirator does not usually suffice. Using a cannula which is positioned right before the defect combined with intraluminal insertion of an extended compress into this cannula with the help of foreceps has paid off. The compresse's wicking action normally alows for sufficient drying of the defect.

Preparation and application of ChondroFiller^{liquid}

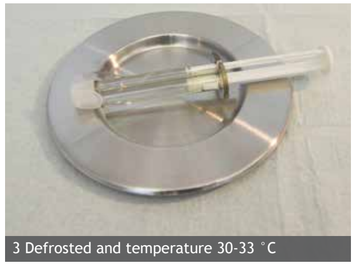
After confirming the indication for carrying out the ChondroFiller^{liquid} method the appropriate syringe should be defrosted. It can be thawed within 24 h at 2-10 °C or immediately before use. The immediate thawing process takes approx. 30 min at an optimal temperature of approx. 25-30 °C (heating cabinet). Right before application the ChondroFiller^{liquid} syringe must be warmed to 30–33 °C (heating cabinet) for a short time (< 15 min).

Warming temperatures of 30–33 °C > 15 min and temperatures higher than 33 °C lead to irreversible collagen damage so that a matrix stabilisation can not occur!

Placing the luerlock mixing adapter is only possible in one position (“nose to nose” – click sound). After placing an injection needle (e.g. G 20 x 2 ¾ single-injection-cannula Sterican®, article number 4665791, B. Braun, Melsungen AG, Germany) the first microliters of the primary liquid matrix have to be discarded before the actual injection (Fig. 2. pic 1-6).


1 ChondroFiller^{liquid}-Set


2 Frozen


3 Defrosted and temperature 30-33 °C


4 + Luerlock mixing adapter


5 + Injection cannula

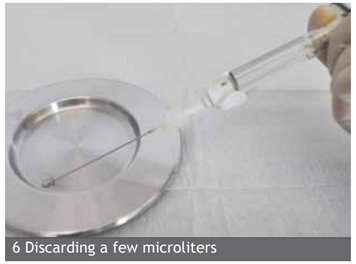

6 Discarding a few microliters

Fig. 2 Preparation ChondroFiller^{liquid}

Surgical technique ChondroFiller^{liquid}

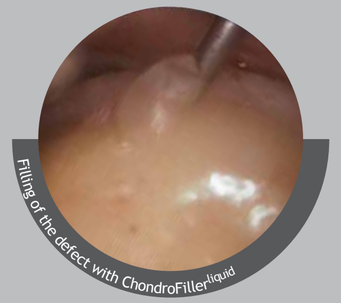
Preparation and application of ChondroFiller^{liquid} continued

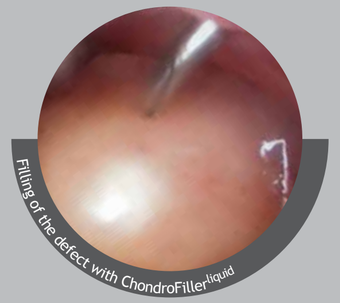
Subsequently the defect should be filled as quickly as possible (< 10 sec) and without interruptions because of the immediate reaction of the two components. The faster the components are pressed through the mixing adapter the better the matrix stabilisation results are. The cartilage defect is filled complete and minimally beyond the height of the surrounding cartilage with the collagen matrix (Fig. 3). The matrix stabilisation takes approx. 2-3 min at an optimal processing temperature of approx. 30-33 °C. This stabilisation is optically visible. The primary transparent gel gets milky haze.

If the processing temperature of 30-33 °C is not achieved, the matrix stabilisation time increases significantly (e.g. 25-30 °C ➔ 10 min). During this time the treated extremity should not be moved. Vibrations can inhibit the implant matrix stabilisation.

The height of the implant can adapted to the height of the surrounding cartilage either manually or automatically through the corresponding articular surface's pressure.
Then the extremity is gently transferred into the extended operating position and access channels can be closed. The insertion of a drain usually is not necessary. Reviewing the defect filling should be avoided if possible as bleeding into the joint prevents a clear view of the implant. Renewed swelling of the joint carries the risk of implant replacement. Through a close-knit MRI-monitoring of all patients who have been treated with this method a secure retention of the implanted gel has been detected in all cases so far.
After applaying wound bandages the treated joint should be immobilized with a brace for 48 hours in a neutral position.

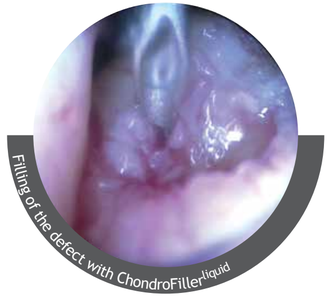
Arthroscopy with irrigation fluid





Filling of the defect with ChondroFiller^{liquid} processing temperature 30-33 °C after drying the defect zone

Arthroscopy with gas (CO_2)



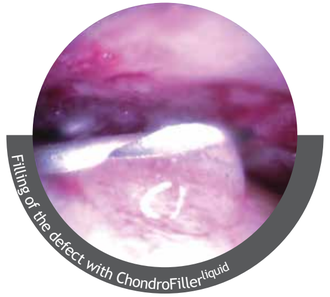


Fig. 3 Application ChondroFiller^{liquid}

Surgical technique ChondroFiller[liquid]

Patient

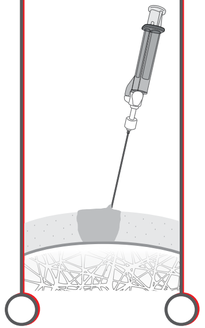
Result arthroscopy:

Indication for ChondroFiller[liquid] treatment given

Debridement of the defect; if necessary change the bearing of the patient

Drying of the defect zone

Filling of the defect as quickly as possible (< 10 sec)



Matrix stabilisation within 2-3 min without vibrations and at optimal processing temperature of 30-33 °C

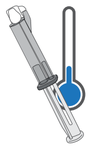
Adaption of the implant height through the pressure of the corresponding articular joint; when indicated manual adaption possible

Transferring the extremity into the extended operating position

Closing of the access channels

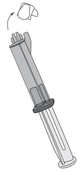
ChondroFiller[liquid]

Thawing prior to immediate use (approx. 30 min in heating cabinet) or alternatively within 24 h prior to surgery at 2-10 °C



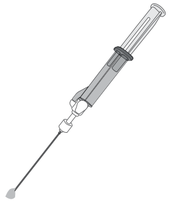
Warming to optimal processing temperature 30-33 °C (< 15 min in heating cabinet)

Removal of the closing cap



Placing of the luer-lock mixing adapter and the injection cannula

Discarding a few microliters of the primary liquid matrix



After treatment

The post-operative treatment

The treatment is mainly determined by the anatomic location of the defect in the joint. There are two basic ways: 1. defects are located in the main load area of the joint and are thus subjected to axial load and 2. defects that are located on the patella or at the corresponding articular surface, e.g. at the femoral trochlea, and loaded only during flexion of the joint. In both cases the rehabilitation program is based on the respective recommendations of the professional societies for trauma surgery DGU and orthopedics DGOOC (Pietschmann, 2012):

Main loading zone of the femoral condyles/talus:

- Mobilization at day 2 post-operative
- 20 kg partial weight bearing on the operated limb for 6 weeks
- Exercise bar (CPM) at least twice a day for 1 hour
- From the 7th week on load up to 30 kg, 2 weeks to full weight bearing
- After reaching full load capability cycling and swimming are allowed, careful muscle formation through isometric training
- Jumping, running and contact sports are allowed after 1 year

Patella and retropatellar bearings:

- Mobilization on day 2 post-operative
- The knee flexion is limited by an IROM-rail for 3 weeks on 0-0-30°
- 20 kg partial weight bearing on the operated limb for 1 week
- From the 2nd week full load allowed
- After the 3rd week increase in flexion to 30° every 2 weeks, from 90° of flexion the IROM-rail will be removed
- After reaching 90° flexion cycling and swimming are allowed, careful muscle formation through isometric training
- Sports with a high risk of falls are allowed after 1 year

Literature

Andereya S, Maus U, Gavenis K, Muller-Rath R, Miltner O, Mumme T, Schneider U (2006) First clinical experiences with a novel 3D-collagen gel (CaReS) for the treatment of focal cartilage defects in the knee. Z Orthop Ihre Grenzgeb 144:272–280

Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L (1994) Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. N Engl J Med 331:889–895

Efe T, Theisen C, Fuchs-Winkelmann S, Stein T, Getgood A, Rominger MB, Paletta JR, Schofer MD (2012) Cell-free collagen type I matrix for repair of cartilage defects-clinical and magnetic resonance imaging results. Knee Surg Sports Traumatol Arthrosc. Oct;20(10):1915-22. Epub 2011 Nov 18.

Gavenis K, Schmidt-Rohlfng B, Andereya S, Mumme T, Schneider U, Mueller-Rath R (2010) A cell-free collagen type I device for the treatment of focal cartilage defects. Artif Organs 34:79–83

Pietschmann M F, Horng A, Glaser C, Albrecht D, Bruns J, Scheffer S, Marlovits S, Angele P, Aurich M, Bosch U, Fritz J, Frosch KH, Kolombe T, Richter W, Petersen J P, Nöth U, Niemeyer P, Jagodzinsky M, Kasten P, Ruhnau K, Müller PE (2012) Post-treatment rehabilitation after autologous chondrocyte implantation : State of the art and recommendations of the clinical tissue regeneration study group of the German Society for Accident Surgery and the German Society for Orthopedics and Orthopedic Surgery.Unfallchirurg. 2012 Nov 25.

Schneider U, Schmidt-Rohlfng B, Gavenis K, Maus U, Mueller-Rath R, Andereya S (2011) A comparative study of 3 different cartilage repair techniques. Knee Surg Sports Traumatol Arthrosc. Dec;19(12):2145-52.

Schneider U, Rackwitz L, Andereya S, Siebenlist S, Fensky F, Reichert J, Löer I, Barthel T, Rudert M, Nöth U (2011) A prospective multicenter study on the outcome of type I collagen hydrogel-based autologous chondrocyte implantation (CaReS) for the repair of articular cartilage defects in the knee. Am J Sports Med. 2011 Dec;39(12):2558-65.

Schüttler KF, Schenker H, Theisen C, Schofer MD, Getgood A, Roessler PP, Struewer J, Rominger MB, Efe T. Use of cell-free collagen type I matrix implants for the treatment of small cartilage defects in the knee: clinical and magnetic resonance imaging evaluation. Knee Surg Sports Traumatol Arthrosc. 2013 Nov 7

This surgical instruction serves as an educational tool for the clinical support of medical professionals to use specific Amedrix products. Finally medical professionals decide about the technique and how to use the product. Medical professionals should act corresponding to their education and experience and refer to medical literature or the instruction for use.

ChondroFiller[liquid]

AMEDRIX

Producer:

Amedrix GmbH
Schelztorstr. 54-56
D-73728 Esslingen
info@amedrix.de, www.amedrix.de