



IMPLANTATION OF CHONDROFILLER LIQUID® AS A SCAFFOLD MATERIAL FOR THE TREATMENT OF CHONDRAL LESIONS OF THE KNEE JOINT

Emil Simeonov

Department of Orthopaedics and Traumatology, Faculty of Medicine, Medical University – Pleven, Bulgaria.

ABSTRACT

Introduction: Trauma, sports, or the normal aging degenerative process may damage the articular cartilage. Surgical methods that are most often used to manage cartilage defects include autologous chondrocyte implantation, mosaicplasty, microfractures, perforations, and joint arthroplasty in cases of severe damage. Another approach is to use collagen gel for cartilage defect reconstruction. Its biocompatibility, high tensile strength, and minimal invasiveness make it an attractive solution. ChondroFiller gel is a two-component collagen implant that could be used in the treatment of traumatic or degenerative chondral lesions. After application, it forms a protective cover for the damaged chondral area and provides structural support for the stem cells that migrate to its collagen matrix. Thus, with ChondroFiller, we aim to restore articular cartilage, prevent further degenerative processes, and return to normal joint function. In this research, we have investigated the application of ChondroFiller during knee arthroscopy to treat knee articular cartilage lesions.

Methods: The clinical study was conducted at the University Hospital—Pleven Clinic of Orthopedics and Traumatology between 2012 and 2023. Seventeen patients (ten males and seven females) with a mean age of 31 years underwent knee chondroplasty with ChondroFiller gel, and their data was analyzed. Knee function was assessed using the Lysholm scale and IKDC score. The follow-up period was twelve months.

Results: Statistical analysis has shown a significant difference between pre-operative Lysholm and pre-operative IKDC score and 3rd month, 6th and 12 months. Significant difference is detected between the 3rd month and 6th and 12th months Lysholm and IKDC scores ($p < 0.05$). No statistical difference was found between 6 and 12 month ($p > 0.05$).

Conclusion: Restoring joint congruity is challenging. Overall, we have found encouraging results by employing ChondroFiller to restore articular cartilage. We believe that Chondrofiller provides an excellent surgical solution to younger patients with chondral defects less than 2cm². In our opinion, further research in the field of collagen implants is needed to discover long-term effect.

Keywords: Cartilage repair, Knee Joint, Articular Cartilage, Acellular scaffolds,

INTRODUCTION

Currently, no universal technology exists for the repair of cartilage defects that is suitable for all patients [1]. Various techniques have been discussed, including microfracture, perforation, mosaicplasty, and autologous chondrocyte implantation, among others [1, 2]. Each of these methods was developed with the primary goal of reconstructing cartilage. However, the underlying biological challenge lies within the nature of cartilage itself [3]. Unlike many other tissues in the body, which possess a significant capacity for recovery or at least the formation of scar tissue, hyaline cartilage lacks this ability due to its avascular nature and the limited mitotic potential of chondrocytes [4]. Consequently, after surgical intervention, the injured area is typically covered by fibrous cartilage, which does not possess the same mechanical properties as hyaline cartilage and is more susceptible to degenerative changes [6]. Over time, this can lead to joint degeneration, which will ultimately necessitate arthroplasty.

To address this biological challenge, we need to find a biological solution. One such approach involves the use of an absorbable acellular collagen implant [7]. Ideally, after application, this collagen implant would provide a matrix for multipotent stem cells and chondrocytes, facilitating their migration and differentiation [8, 9]. It should also replicate the natural biological and mechanical properties of hyaline cartilage while providing mechanical support for the migrating cells [8, 9, 10]. At the same time, as a bioabsorbable material, it should also be gradually replaced by newly formed hyaline cartilage [11].

Chondrofiller is an example of an absorbable acellular collagen implant. When applied to the focal area of a cartilage lesion, it forms a protective layer over the injured area and provides a matrix for the migration of stem cells from bone marrow. Promising results have been reported in both in-vitro and in-vivo studies. The purpose of this study was to investigate the use of ChondroFiller liquid® in the arthroscopic treatment of focal articular cartilage lesions of the knee.

METHODOLOGY

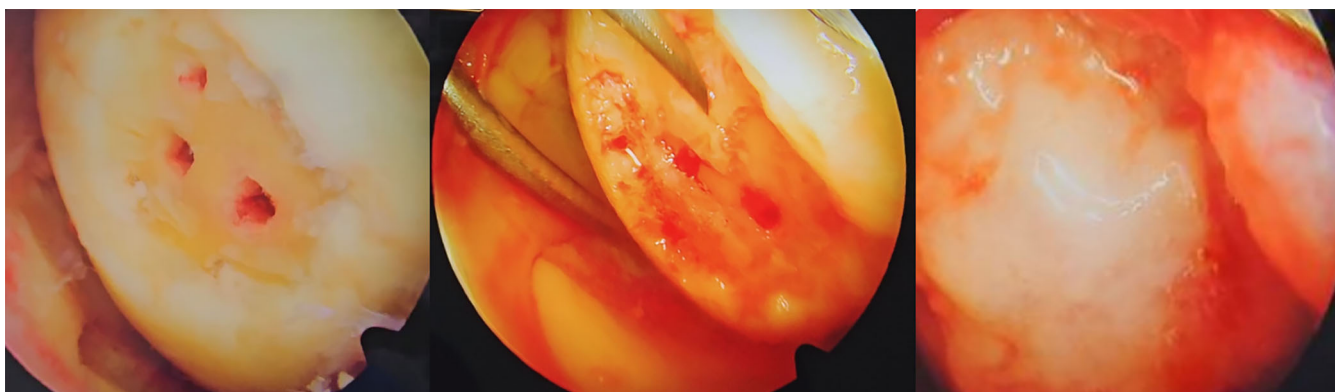
The clinical study was conducted at the University Hospital—Pleven, within the Clinic of Orthopedics and Traumatology. The study includes patient data from 2012 to 2023. Twenty-two patients underwent knee chondroplasty with ChondroFiller liquid. Five patients missed their follow-up appointments and thus were excluded from the analysis. Thus, the data of seventeen patients (ten males and seven females) were analyzed. Each patient provided written informed consent prior to surgery. The follow-up period for the study was twelve months. Knee function was evaluated using the Lysholm scale and IKDC score.

The exclusion criteria included: under 18 years old, over 65 years old, previous history of chondroplasty surgery and Kellgren-Lawrence grade ≤ 2 .

Each patient received a dose of Enoxaparin 6000E (Fraxiparine) 12 hours before the surgery, and deep vein thrombosis (DVT) prophylaxis was continued for 15 days postoperatively.

Knee arthroscopy was performed in a standardized, systematic manner as outlined by Ward and Lubowitz (2013) [12]. Each patient was operated by the same surgeon. Upon visualizing the defect, its size was carefully measured using a probe, and the area was prepared. The preparation process involved careful debridement using a curette and a shaver. Microfracturing was then carried out using the technique originally described by Steadman et al. Following this, the arthroscopic saline solution was evacuated from the knee joint, and a cotton swab was used to further dry the area of the chondral lesion. Chondrofiller liquid was implanted using a spinal needle [Fig 1]. The gelification of the implant was assessed visually. At the completion of the gelification, the gel was gently checked with the probe. Postoperatively, the operated limb was immobilized with a knee orthosis for 48 hours in a flexed position (35 degrees). Patients were permitted to gradually begin applying weight to the operated limb four weeks after surgery. Full weight-bearing and the resumption of sports activities were allowed six months post-surgery.

Fig. 1. Application of Chondrofiller liquid on the prepared area.



STATISTICAL ANALYSIS AND RESULTS

All data was checked for normal distribution by the Kolmogorov-Smirnov test. The alpha level of significance was set to 0.05. One-way repeated measures ANOVA with Tukey post-hoc test was used to analyze data. Statistical analysis was performed using Minitab® version 22.1 and Microsoft Office 2021.

Data from seventeen patients (10 males and seven females) were analyzed. The average age of the patients was 31 ± 4 . The average defect size was $2.3 \pm 0.73 \text{ cm}^2$.

Fig. 2. Probability plot of patient age. Normal distribution ($p > 0.150$).

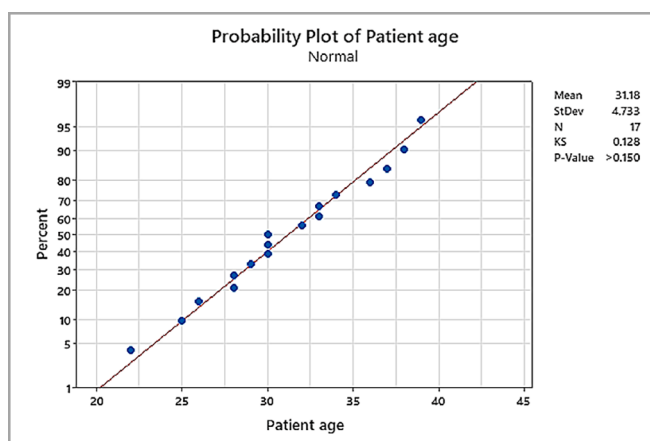
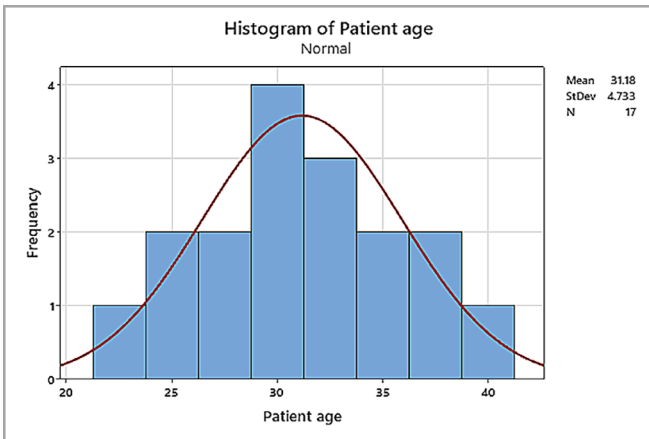
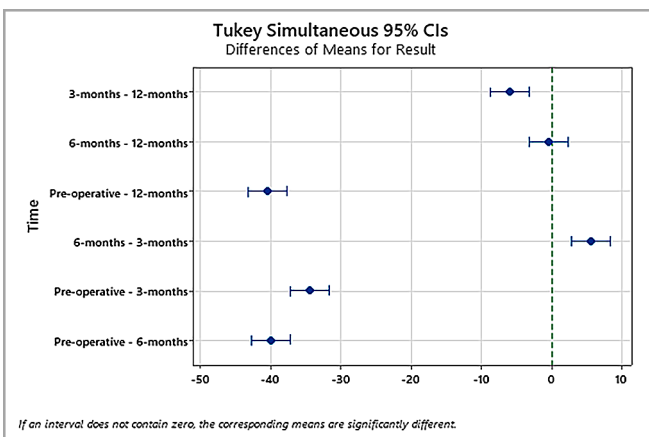


Fig. 3. Histogram of patient age.



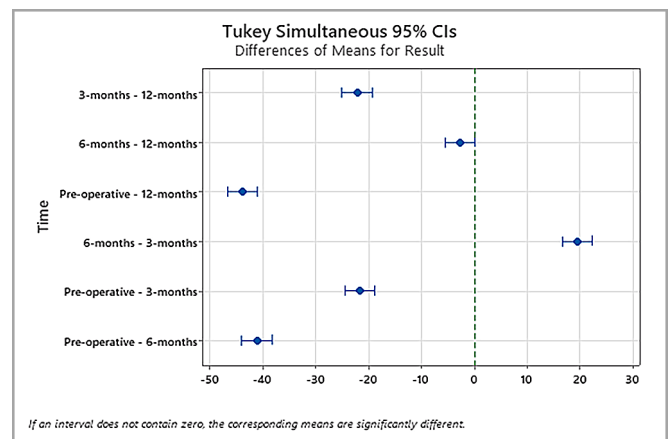
Data was found to be normal according to the Kolmogorov-Smirnov test. Statistical analysis has shown a significant difference between pre-operative Lysholm score and 3rd month, 6th and 12 months. Significant difference is detected between the 3rd month and 6 and 12 months Lysholm score ($p < 0.05$). No statistical difference was found between 6 and 12 month ($p > 0.05$).

Fig. 4. Statistical analysis of Lysholm score.



Statistical analysis has shown a significant difference between pre-operative Lysholm score and 3rd month, 6th and 12 months. Significant difference is detected between the 3rd month and 6 and 12 months Lysholm score ($p < 0.05$). No statistical difference was found between 6 and 12 month ($p > 0.05$).

Fig. 5. Statistical analysis of IKDC score.



Statistical analysis has shown a significant difference between pre-operative IKDC score and 3rd month, 6th and 12 months. Significant difference is detected between the 3rd month and 6 and 12 months Lysholm score ($p < 0.05$). No statistical difference was found between 6 and 12 month ($p > 0.05$).

DISCUSSION

Restoration of cartilage defects still remains a major obstacle in orthopedics [12]. Lots of research has been focused during the last decade to finding suitable biomaterial which could be used.

In their 2011 study, Schneider et al. investigated the effectiveness of a cell-free collagen type-I gel compared to a cell-seeded collagen gel for treating full-thickness chondral defects in an animal model [9]. After one year, both treatment groups exhibited mature hyaline-like repair tissue at the defect site, while the control group developed fibrous tissue. Multivariate analysis of the O'Driscoll score showed no significant differences between the two types of active treatments (cell-free and cell-seeded).

In a separate study, Buma P et al. investigated the implantation of cross-linked type I and type II collagen matrices into chondral defects, both with and without attached chondroitin sulfate [8]. After four weeks, they observed that defects treated with type I collagen-based matrices were almost entirely filled with cartilage-like tissue. In contrast, defects filled with type II collagen exhibited cartilaginous tissue primarily at the interface between the matrix and subchondral bone, as well as superficially. The study also noted that defects treated with type I collagen demonstrated superior histological outcomes. The absence of blood vessels in the defect area led to the hypothesis that the collagen matrix facilitated the migration of mesenchymal stem cells from the

subchondral region, promoting their differentiation into a chondrocytic phenotype. Further support for cell migration from host tissue into the collagen matrix is provided by studies conducted by Schuman L et al., Gavenis K, et al. and Schneider U, et al., although the precise mechanisms behind this phenomenon remain unclear [9, 13, 14]. Additionally, research by Yates K, et al. has shown that collagen matrices create favorable conditions for chondrocytes to maintain viability, morphological integrity, and synthetic activity [15, 16].

In 2016, Schneider U, conducted a study comparing the use of Chondrofiller with the microfracture procedure for treating articular cartilage lesions in the knee [17]. Interestingly, the study reported a high dropout rate among patients in the microfracture group, although specific reasons for these dropouts were not provided; it was mentioned that they occurred following the randomization process. Despite this limitation, MRI investigations after surgery performed after one year indicated complete integration of the collagen implant, with the imaging reportedly revealing an isointense signal that was largely indistinguishable from the surrounding healthy cartilage.

Mazek J, et al. [7] found Chondrofiller to be effective in the treatment of cartilage defects more than 2cm², as evidenced by control MRI evaluation at 6 and 18 months postoperatively. However, they also simultaneously notice and discourage the use of Chondrofiller in patients with Tönnis grade 2 and 3. They suggest that joint space of <2mm and high Tönnis grade should be considered as a contraindication for chondroplasty with Chondrofiller. Whereas a good or excellent score according to the modified Harris Hip Score (mHHS) was obtained in patients with Tönnis grade 0 and 1 lesion, the only poor outcome was seen in 2 patients with Tönnis grade 2. In our opinion, the patients who are subject to knee chondroplasty with Chondrofiller should be with Kellgren-Lawrence grade less than 3.

Von Engelhardt L, et al. discuss the use of Chondrofiller in treating a Grade 4 Outerbridge cartilage defect on the articular surface of the femoral head in a professional athlete [18]. Interestingly, the chondral lesion was discovered incidentally during an arthroscopic surgery initially planned for the removal of an osteoid osteoma. This case is particularly noteworthy as it involved the simultaneous performance of two distinct procedures. The patient was able to return to professional sports within eight months, remaining pain-free and without any further complications.

The inclusion of cells or the use of an acellular

technique, as in our study, remains a topic of ongoing debate [19]. While existing literature provides evidence of mesenchymal stem cell (MSC) migration into hydrogel matrices, there is still a lack of documented long-term outcomes comparing acellular vs cellular-based approaches. Additionally, there is ongoing controversy surrounding the use of microfracture or tunnelization procedures prior to the application of Chondrofiller.

In our study, similar to the work of Schneider U, we utilized the microfracture technique prior to the application of Chondrofiller gel [17]. The rationale behind this approach is that microfractures may enhance the integration of repair tissue with the surrounding cartilage and promote cell migration when used in conjunction with a scaffold implant [20]. However, Strauss E, et al. pointed out that the use of the microfracture technique is predominantly yet limited to animal studies and case reports, such as those published by Erggelet C, et al., Hoemann et al., Zantop and Petersen (2009) [21, 22, 23]. As a result, some researchers, including Engelhardt et al., choose not to use microfracture or tunnelization techniques, in contrast to the approaches taken in our study and Schneider's research.

According to the manufacturer, Chondrofiller must be applied in a dry environment. In our study, we achieved this by evacuating all arthroscopic fluid and using a cotton swab to dry the defect area. However, as demonstrated by Mirzayan R, et al., who utilized CO₂ insufflation instead of saline solution, CO₂ not only provides adequate visualization but also maintains a dry environment [24]. Therefore, employing CO₂ insufflation could enhance the efficiency of the arthroscopic application of Chondrofiller or any other matrix/scaffold. Additionally, it would eliminate, albeit with a low risk of inadvertently leaving cotton swab remnants within the joint. Based on our clinical trial, we recommend using carbon dioxide for joint insufflation during arthroscopy.

A limitation of this study is the absence of a control group. Future research that aims to randomize groups should consider the findings of Schneider U, where a significant number of patients randomly allocated to the microfracture (control) group declined randomization and chose to withdraw from the study [17]. Despite this limitation, our study still demonstrated a statistically significant improvement in the Lysholm and IKDC score over 12 months compared to the pre-operative state.

Overall, we agree with the point of many authors such Buryanov O, et al., Bong and Lee; Strauss E, et al. Schneider U, Mazek J, et al. that further research in this

field is warranted [1, 7, 17, 20, 25]. As pointed by Mazek J, et al., further research should also aim to investigate the long-term effect of free-cell collagen implants [7].

CONCLUSION

Chondral defects could be successfully treated by implantation of cell-free type-I collagen. However, ad-

ditional studies are required to further validate the use of cell-free type-I collagen in mid-term and long-term periods.

Abbreviations

IKDC - International Knee Documentation Committee.

REFERENCES:

1. Buryanov OA, Chorny VS, Bazarov MO, Mohilnytsky AO, Hutsailiuk VI, Kusyak AP, et al. Modern technologies for replacement of cartilage defects. *Trauma*. 2024; 25(3):45-53. [[Crossref](#)]
2. Gracitelli GC, Moraes VY, Franciozi CE, Luzo MV, Belloti JC. Surgical interventions (microfracture, drilling, mosaicplasty, and allograft transplantation) for treating isolated cartilage defects of the knee in adults. *Cochrane Database Syst Rev*. 2016 Sep 3;9(9):CD010675. [[PubMed](#)]
3. Hunziker EB. The elusive path to cartilage regeneration. *Adv Mater*. 2009 Sep 4;21(32-33):3419-24. [[PubMed](#)]
4. Steinert AF, Ghivizzani SC, Rethwilm A, Tuan RS, Evans CH, Nöth U. Major biological obstacles for persistent cell-based regeneration of articular cartilage. *Arthritis Res Ther*. 2007;9(3):213. [[PubMed](#)]
5. Bađenková D, Trebuřová M, Demeterová J, •ivěák J. Human Chondrocytes, Metabolism of Articular Cartilage, and Strategies for Application to Tissue Engineering. *Int J Mol Sci*. 2023 Dec 4;24(23):17096. [[PubMed](#)]
6. Falah M, Nierenberg G, Soudry M, Hayden M, Volpin G. Treatment of articular cartilage lesions of the knee. *Int Orthop*. 2010 Jun;34(5):621-30. [[PubMed](#)]
7. Mazek J, Gnatowski M, Salas AP, O'Donnell JM, Domęalski M, Radzimowski J. Arthroscopic utilization of ChondroFiller gel for the treatment of hip articular cartilage defects: a cohort study with 12- to 60-month follow-up. *J Hip Preserv Surg*. 2021 Jul 31;8(1):22-27. [[PubMed](#)]
8. Buma P, Pieper JS, van Tienen T, van Susante JL, van der Kraan PM, Veerkamp JH, et al. Cross-linked type I and type II collagenous matrices for the repair of full-thickness articular cartilage defects—a study in rabbits. *Biomaterials*. 2003 Aug;24(19):3255-63. [[PubMed](#)]
9. Schneider U, Schmidt-Rohlfing B, Gavenis K, Maus U, Mueller-Rath R, Andereya S. A comparative study of 3 different cartilage repair techniques. *Knee Surg Sports Traumatol Arthrosc*. 2011 Dec;19(12):2145-52. [[PubMed](#)]
10. Zhang H, Wang M, Wu R, Guo J, Sun A, Li Z, et al. From materials to clinical use: advances in 3D-printed scaffolds for cartilage tissue engineering. *Phys Chem Chem Phys*. 2023 Sep 20;25(36):24244-24263. [[PubMed](#)]
11. Wang M, Wu Y, Li G, Lin Q, Zhang W, Liu H, et al. Articular cartilage repair biomaterials: strategies and applications. *Mater Today Bio*. 2024 Jan 6;24:100948. [[PubMed](#)]
12. Simeonov E. Analysis of medium-term results achieved after microfractures and perforations (drilling) in localized chondral lesions in the knee joint. *J of IMAB*. 2023 Jul-Sep;29(3):5125-5135. [[Crossref](#)]
13. Schuman L, Buma P, Versleyen D, de Man B, van der Kraan PM, van den Berg WB, et al. Chondrocyte behaviour within different types of collagen gel in vitro. *Biomaterials*. 1995 Jul;16(10):809-14. [[PubMed](#)]
14. Gavenis K, Schmidt-Rohlfing B, Andereya S, Mumme T, Schneider U, Mueller-Rath R. A cell-free collagen type I device for the treatment of focal cartilage defects. *Artif Organs*. 2010 Jan;34(1):79-83. [[PubMed](#)]
15. Yates KE, Allemann F, Glowacki J. Phenotypic analysis of bovine chondrocytes cultured in 3D collagen sponges: effect of serum substitutes. *Cell Tissue Bank*. 2005; 6(1):45-54. [[PubMed](#)]
16. Ahmed TA, Hincke MT. Strategies for articular cartilage lesion repair and functional restoration. *Tissue Eng Part B Rev*. 2010 Jun;16(3):305-29. [[PubMed](#)]
17. Schneider U. Controlled, randomized multicenter study to compare compatibility and safety of ChondroFiller liquid (cell free 2-component collagen gel) with microfracturing of patients with focal cartilage defects of the knee joint. *J Ortop Surg*. 2016;1:1-8 [[Crossref](#)]
18. von Engelhardt LV, El Tabbakh MR, Engers R, Lahner M, Jerosch J. Hip arthroscopy for excision of osteoid osteoma and for the application of a collagen cartilage implant: Case report in a professional athlete, and literature review. *Technol Health Care*. 2016 Nov 14;24(6):957-964. [[PubMed](#)]
19. Brittberg M. Cellular and Acellular Approaches for Cartilage Repair: A Philosophical Analysis. *Cartilage*. 2015 Apr;6(2 Suppl):4S-12S. [[PubMed](#)]
20. Strauss EJ, Barker JU, Kercher JS, Cole BJ, Mithoefer K. Augmentation Strategies following the Microfracture Technique for Repair of Focal Chondral Defects. *Cartilage*. 2010 Apr;1(2):145-52. [[PubMed](#)]
21. Erggelet C, Endres M, Neumann K, Morawietz L, Ringe J, Haberstroh K, et al. Formation of cartilage repair tissue in articular cartilage defects pretreated with microfracture and covered with cell-free polymer-based implants. *J Orthop Res*. 2009 Oct;27(10):1353-60. [[PubMed](#)]
22. Hoemann CD, Hurtig M, Rossomacha E, Sun J, Chevrier A, Shive MS, et al. Chitosan-glycerol phosphate/blood implants improve

hyaline cartilage repair in ovine microfracture defects. *J Bone Joint Surg Am.* 2005 Dec;87(12):2671-2686. [[PubMed](#)]

23. Zantop T, Petersen W. Arthroscopic implantation of a matrix to cover large chondral defect during microfracture. *Arthroscopy.* 2009

Nov;25(11):1354-60. [[PubMed](#)]

24. Mirzayan R, Cooper JD, Chahla J. Carbon Dioxide Insufflation of the Knee in the Treatment of Full-Thickness Chondral Defects With Micronized Human Articular Cartilage. *Arthrosc Tech.* 2018 Sep 1;7(10):e969-e973. [[PubMed](#)]

25. Bong G, Lee Y. Injectable Scaffold with Microfracture using the Autologous Matrix-Induced Chondrogenesis (AMIC) Technique: A Prospective Cohort Study. *Malays Orthop J.* 2022 Nov;16(3):86-93. [[PubMed](#)]

Please cite this article as: Simeonov E. Implantation of ChondroFiller Liquid® as a scaffold material for the treatment of chondral lesions of the knee joint. *J of IMAB.* 2024 Oct-Dec;30(4):5936-5941. [Crossref - <https://doi.org/10.5272/jimab.2024304.5936>]

Received: 23/09/2024; Published online: 17/12/2024



Address for correspondence:

Dr Emil Simeonov, MD, PhD
Clinic of Orthopaedics & Traumatology, UMBAL “Dr. Georgi Stranski “-
Pleven;
89, Ruse Blvd., Pleven 5803, Bulgaria.
E-mail: emil.simeonov.pl@gmail.com,