fortune Journals

Case Study

JOURNAL OF ORTHOPAEDICS AND SPORTS MEDICINE

ISSN: 2688-5115

Hydrogel alone or in Combination with Regenerative Interventions for Knee Osteoarthritis, A Case Series

Torbjörn Ogéus DC, PgD, MSc, ScA*

Abstract

Introduction: Osteoarthritis (OA) of the knee is one of the most prevalent degenerative joint diseases worldwide, contributing to chronic pain, reduced mobility, and diminished quality of life. As the primary weight-bearing joint, the knee is particularly susceptible to OA, especially in older adults and those with a history of joint injury or obesity.

Hydrogels have garnered significant attention as a minimally invasive treatment option for knee OA. Hydrogels are water-rich, three-dimensional polymer networks that mimic the natural composition and function of cartilage, making them suitable for use as cushioning agents in the joint. A particular approach is the use of polyacrylamide hydrogel injections, which are non-biodegradable and designed to provide long-lasting pain relief by acting as a viscoelastic buffer within the joint.

Case presentations: Four patients both male and female, all with chronic pain and reduced physical function due to osteoarthritis of the knee. All four showed a remarkable reduction in pain and increase in function after a combination of hydrogel and regenerative interventions such as stem cells, exosomes or platelet injections.

Conclusion: These cases raise the hypothesis that hydrogel has a promising function and pain reduction capacity, especially in combination with regenerative medicine interventions. Some indications show that hydrogel might work as a scaffold for other regenerative interventions. Further research is required to test this theory.

Keywords: PRF; ALB-PRF; Osteoarthritis; Regenerative medicine; Hydrogel; Arthrosamid

Abbreviations: OA: Osteoarthritis; PRF: Platelet Rich Fibrin; NSAIDs: nonsteroidal anti-inflammatory drugs; PPP: platelet-poor plasma; ALB-PRF: heat coagulated albumin-PRF; L-PRF: Liquid PRF; C-PRF: Concentrated PRF; NRS: Numerical Rating Scale.; WOMAC: Western Ontario and McMaster Universities Arthritis Index; IV: intravenously.

Introduction

Osteoarthritis (OA) of the knee is one of the most prevalent degenerative joint diseases worldwide, contributing to chronic pain, reduced mobility, and diminished quality of life. As the primary weight-bearing joint, the knee is particularly susceptible to OA, especially in older adults and those with a history of joint injury or obesity [1]. Conventional treatments for knee OA include nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroid

Affiliation:

Stockholms led- & smärtklinik, 11424, Stockholm, Sweden

***Corresponding Author:**

Torbjörn Ogéus, Stockholms led- & smärtklinik, 11424, Stockholm, Sweden.

Citation: Torbjörn Ogéus. Hydrogel alone or in Combination with Regenerative Interventions for Knee Osteoarthritis, A Case Series. Journal of Orthopedics and Sports Medicine. 7 (2025): 16-22

Received: January 08, 2025
Accepted: January 15, 2025
Published: January 24, 2025

Torbjörn Ogéus DC, et al., J Ortho Sports Med 2025
DOI:10.26502/josm.511500176

injections, and physical therapy, which primarily focus on symptom management without effectively slowing disease progression [2]. These limitations drive the need for advanced treatments, such as biomaterial-based interventions, that offer not only symptom relief but also the potential for long-term joint preservation.

Hydrogels have garnered significant attention as a minimally invasive treatment option for knee OA. Hydrogels are water-rich, three-dimensional polymer networks that mimic the natural composition and function of cartilage, making them suitable for use as cushioning agents in the joint [3]. A particular approach is the use of polyacrylamide hydrogel injections, which are non-biodegradable and designed to provide long-lasting pain relief by acting as a viscoelastic buffer within the joint. This type of hydrogel is unique in its structure and mechanical properties, allowing it to integrate with the joint environment without rapid degradation or the need for frequent reinjections [4].

The mechanism of action of polyacrylamide hydrogels is both mechanical and biological. Mechanically, the hydrogel acts as a shock absorber, redistributing forces across the joint and alleviating stress on worn cartilage, which can reduce pain and preserve function [5]. Its durable nature allows it to remain in the joint for an extended period, thus providing sustained relief from OA symptoms. Biologically, polyacrylamide hydrogels have been shown to interact minimally with surrounding tissues, reducing the inflammatory response often associated with other injectable materials [6]. This low inflammatory profile, combined with the hydrogel's cushioning effect, positions polyacrylamide hydrogel injections as a promising alternative to standard treatments for knee OA.

In recent studies, patients receiving polyacrylamide hydrogel injections reported improvements in pain, mobility, and overall joint function, with some findings suggesting a reduced need for more invasive procedures, such as knee replacement [7]. However, while polyacrylamide hydrogels hold promise, further research is needed to establish long-term efficacy, optimal dosing, and potential side effects and the positive effects are typically seen only in early stages of OA [8]. Additionally, as regulatory approval processes for new biomaterials can be complex, the widespread clinical adoption of these treatments may require further refinement and validation.

This case-series study presents unique data indicating a synergistic effect of regenerative interventions combined with the beforementioned polyacrylamide hydrogel that might increase the effectiveness even in cases of more advanced osteoarthritis where hydrogel usually have fewer positive results.

Case Presentations

Case 1

Our first patient was a 57-year-old man who presented at the clinic with prolonged intermittent inflammatory pain. He had received a stem cell and platelet rich fibrin (PRF) treatment two years earlier, and even though the radiographic pictures showed significant healing he was still struggling with pain and swelling of the knee, especially after strenuous activity such as padel or tennis that he used to play. He reported that he experienced pain between 5 and 7 on the numerical rating scale (NRS) daily. His total Western Ontario and McMaster Universities Arthritis Index (WOMAC) score was 33 on the day of treatment.

Case 2

Our second patient was a 32-year-old woman with daily problems of swelling and pain of the knee, she had gone through a PRF-treatment series 1 year earlier and was feeling better, but still had problems with swelling and pain even after low impact activities such as power walking and reported that her pain level was constantly between 2 and 4 on the NRS scale.

Her total WOMAC score was 35 on the day of treatment.

Case 3

Our third patient was a 57-year-old woman with a history of chronic pain in her knee with rather moderate osteoarthritis according to radiographic pictures. She experienced pain at nighttime and swelling after exercise activities such as golf and padel that she had to quit before she presented at the clinic. She reported a pain level between 1 and 6 on the NRS scale and her total WOMAC score was 24 on the day of treatment.

Case 4

Our fourth patient was a 46-year-old man with chronic pain since many years, he had experienced an increase in inflammatory symptoms with pain and swelling after physical activities in the last year. He reported a pain of 3-7 on the NRS scale and his total WOMAC score on the day of treatment was 34.

All four cases had similar injuries and anamnesis, two of the patients had received prior treatment with regenerative interventions such as stem cells or platelet injections. The other two had similar symptoms and injuries to the cartilage of the knee but had not received any biological treatment prior to the hydrogel treatment. The first two cases received hydrogel treatments for their conditions, the last two cases received a combined treatment of platelets, exosomes and hydrogel. All four patients received a combination of treatments including biological regenerative interventions combined with hydrogel, but with different time frames.

Torbjörn Ogéus DC, et al., J Ortho Sports Med 2025
DOI:10.26502/josm.511500176

Materials and Method

Various types of autologous platelet concentrations and injection types have been proposed to be used to treat osteoarthritis and cartilage defects. Prior studies from our clinic have indicated a positive effect on pain, function and stiffness symptoms. Especially where a combination of techniques was used [9,10]. One way of extending the effect of the injected platelets is to heat a liquid platelet-poor plasma (PPP) layer, the resorption properties of heated albumin (albumin gel) can thereby be extended from 2 weeks to more than 4 months (ALB-PRF) [11].

Exosomes derived from stem cells can recapitulate the potential of their parent cells and have therefore been proposed as a substitute for cell therapy to achieve a cell-free therapy option [12,13]. Different routes of administration have been evaluated and the most common route in preclinical studies was the intravenous (IV) injection [14].

Preparation of PRF, ALB-PRF and exosomes

40ml blood was collected from the patients before each of the PRF injections. Four 10ml Plastic, round-bottomed vacuum tubes were used to collect the blood, after collection the tubes were spun on a horizontal swing-out bucket rotors centrifuge system. Two PRF protocols were utilized in the treatment in this case series including a Concentrated-PRF (C-PRF) protocol of 2000×g for 8 min and a Heat-Coagulated Albumin Gel -PRF (ALB-PRF) protocol of 2000×g for 8 min followed by a heating and cooling down process before injection was performed. The two protocols were utilized following international guidelines for PRF preparation published by Miron et al. in 2019 [15].

The PRF injections consisted of concentrated Platelet Rich Fibrin (C-PRF) [16] injection of 4ml, centrifuged at 2000×g for 8 min. While ALB-PRF injections given were 5ml ALB-PRF, 2000×g for 8 min on a horizontal centrifuge, the albumin layer was heated according to the ALB-PRF protocol; 75 degrees for 10 min [17]. In the last step, the heat- coagulated albumin gel was cooled down to room temperature and mixed with the remaining C-PRF to create ALB-PRF. The centrifuge utilized in all PRF treatments was the Bio-PRF horizontal centrifuge (Bio-PRF, USA).

The Exosomes used were 4 trillion amniotic derived exosomes in a 1,5ml extracellular matrix (The center for Regenerative Medicine Laboratories, Miami, USA), in case 3 and 4 half of the matrix was diluted with 5 ml Saline for intravenous injection, while the other half was combined with PRF for intra-articular injection.

Administration of polyacrylamide hydrogel

In all 4 cases six 1 ml polyacrylamide hydrogel syringes of Arthrosamid™ (Contura international A/S, Soeborg, Denmark) were injected intraarticularly into the affected knees using the lateral suprapatellar portal with a 18G, 50mm cannula using ultrasonic guidance. The injection area was anaesthetized with 2ml of lidocaine 20mg/ml. One hour prior to the injections 750mg of Flucloxacillin were given orally.

In case 3 and 4 the polyacrylamide hydrogel was injected first following the same protocol as described above, PRF combined with exosomes was injected directly after using a 3-way luer lok connector.

Administration of PRF and ALB-PRF

The patients in both case 3 and case 4 underwent a series of intra-articular C-PRF and ALB-PRF injections in the osteoarthritic joints. The first injection was combined with the hydrogel as described before, after one week one more intra-articular injection of the ALB-PRF type was performed. All intra-articular joint injections were performed with ultrasound guidance to ensure needle placement inside the joint capsule.

Administration of the exosomes

In case 3 and 4 the exosomes were divided in half, where half of the injection was intra-articular in the osteoarthritic joint combined with a C-PRF injection and half of the exosomes were diluted in saline for a systemic injection intravenously (IV) using the IV-Push technique [18]. no allergic or adverse reactions were observed after any of the injections.

Instruments

The Western Ontario and McMaster Universities Arthritis Index (WOMAC) instrument evaluates three dimensions (pain, stiffness, and physical function) it uses 24 items: pain (5), stiffness (2) and physical function (17) items. It produces three subscale scores, one for each dimension, and a total index score [19]. The WOMAC version used in this study uses a scale of 0–4, with lower scores indicating lower levels of symptoms or physical disability. Each subscale is summarized to a maximum score of 20, 8, and 68 score points, for pain, stiffness and physical function respectively. WOMAC total index score or global score is usually calculated by summarizing the scores for the 3 dimensions [20]. The questionnaire is self-administered and takes approximately 5–10 min to complete.

Results

Case 1

6 months after the hydrogel-treatment he reported that he experienced pain between 0 and 1 on the numerical rating scale (NRS) daily. His total WOMAC score was 8 at the 6-month mark. He reported that he was not bothered anymore when exercising, he was back to playing padel and tennis and reported that his pain and function didn't affect his life anymore.

Torbjörn Ogéus DC, et al., J Ortho Sports Med 2025
DOI:10.26502/josm.511500176

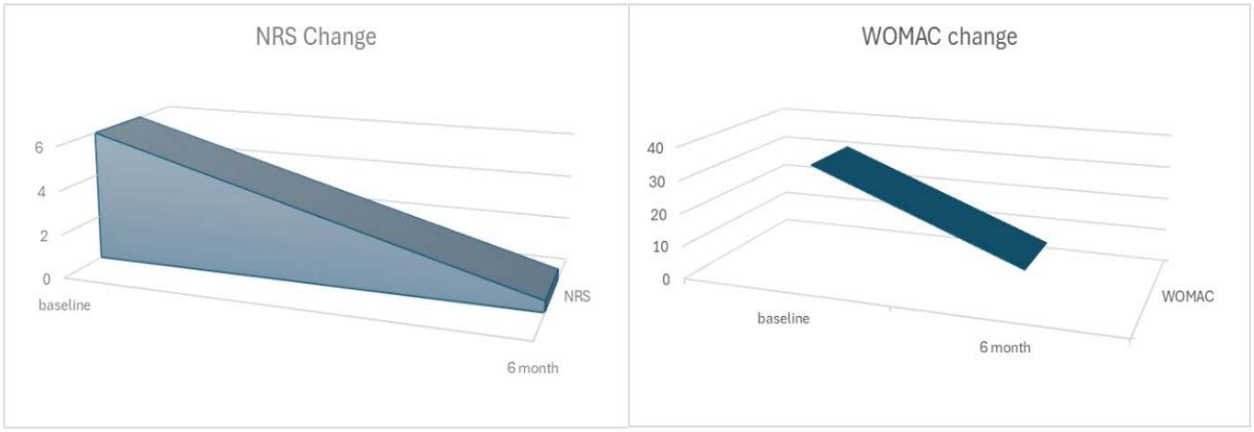

Figure 1: Changes in NRS-score, from 6 to 0.5 (91%) and total WOMAC score, from 33 to 8 (75%) 6 months after the treatment.

Case 2

6 months after the hydrogel-treatment, the patient reported that "all former swelling of the knee was gone". Training activities were no longer causing problems, and she reported that she "experienced no pain at all" on the NRS scale in her daily life. Her total WOMAC score was 2, 6 months after the treatment.

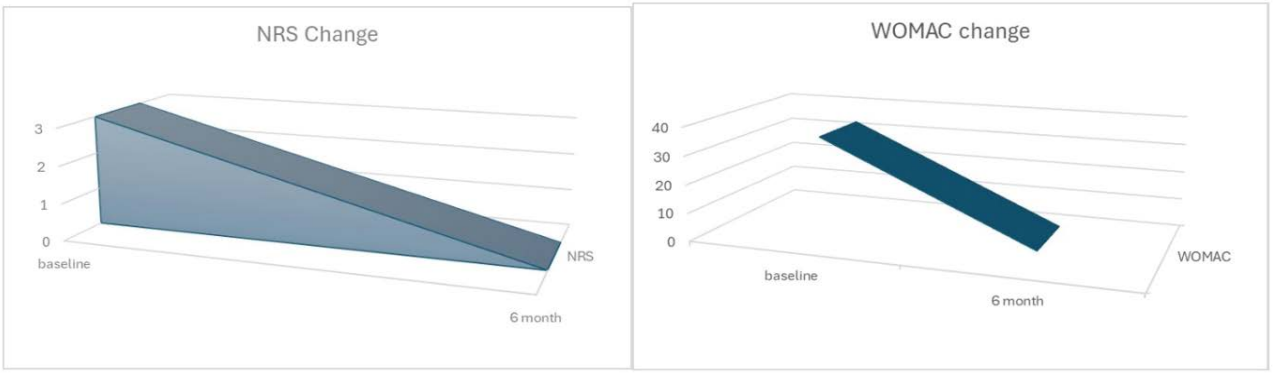

Figure 2: Changes in NRS-score, from 3 to 0. (100%) and total WOMAC score, from 35 to 2 (94%) 6 months after the treatment.

Case 3

6 months after the PRF, exosomes and hydrogel treatment she reported that she hadn't experienced any pain after exercise, she was back to her former sporting activities golf and padel and reported that she was pain free during the night and sleep. She reported an average pain of 1 on the NRS scale and her total WOMAC score was 3 at the 6-month follow-up visit.

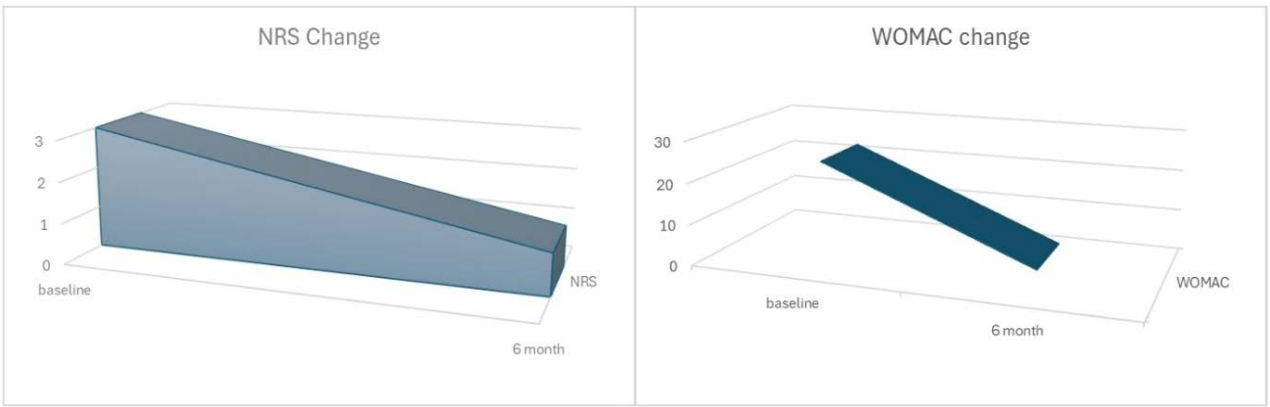

Figure 3: Changes in NRS-score, from 3 to 1 (67%) and total WOMAC score, from 35 to 2 (88%) 6 months after the treatment.

Torbjörn Ogéus DC, et al., J Ortho Sports Med 2025
DOI:10.26502/josm.511500176

Case 4

At the 6-month follow-up visit our fourth patient reported that he was virtually pain free after physical activities and all his former swelling was gone. His total WOMAC score changed from 34 to 4. Case 3 and 4 were the first time in Europe that patients received a combined treatment of Hydrogel, PRF and exosomes at the same time instead of going through a staged approach of treatment reported in the first two cases in this case series.

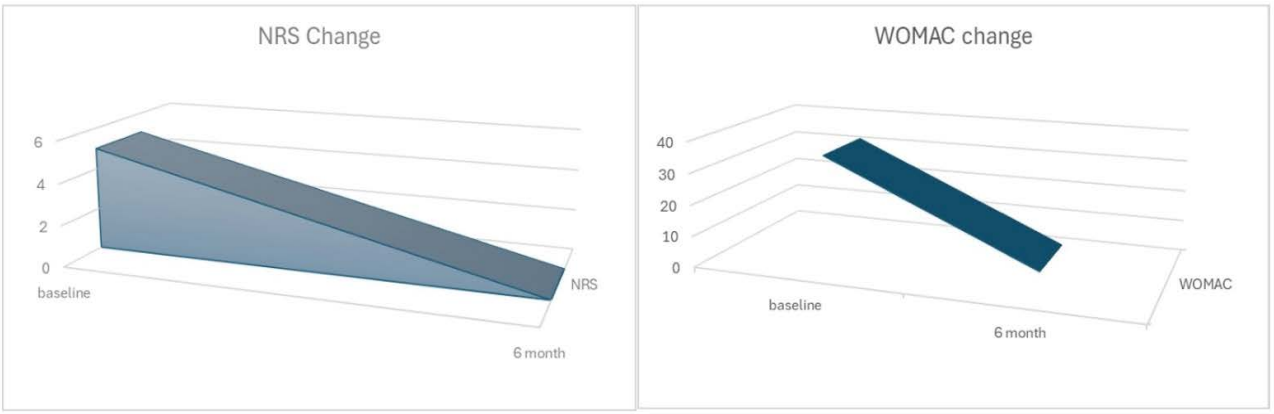

Figure 4: Changes in NRS-score, from 5 to 0 (100%) and total WOMAC score, from 35 to 2 (94%) 6 months after the treatment.

Discussion

The use of hydrogels as adjunctive or combination therapy with biologic treatments, such as stem cell and platelet-rich fibrin injections, is an emerging area of interest in managing knee osteoarthritis. While stem cell and PRF injections aim to promote tissue repair and regeneration through cellular and growth factor delivery, polyacrylamide hydrogels offer an opportunity to enhance these effects by acting as a scaffold that sustains and stabilizes the injected cells and growth factors [21]. When used in combination, hydrogels can provide a more supportive microenvironment that encourages cellular attachment, proliferation, and matrix deposition, thereby potentially improving the therapeutic outcomes [22].

Polyacrylamide hydrogels can be engineered to have properties that complement biologic therapies. For instance, their high-water content and viscoelastic properties allow them to act as a cushioning material, which is beneficial for stabilizing the knee joint while allowing gradual cellular and tissue integration [23]. Hydrogels may prolong the residence time of stem cells or platelets in the joint, which could lead to more sustained release of anti-inflammatory factors and growth factors, enhancing the regenerative response [24,25].

Early clinical studies have demonstrated the benefit of combining hydrogels with platelet concentrate-injections in cartilage regeneration. PRF is rich in growth factors that stimulate chondrocyte proliferation and extracellular matrix synthesis and pairing it with a hydrogel scaffold can maintain PRF within the joint for longer periods, potentially leading to improved cartilage repair and reduced degradation rates [26,27]. Similarly, in stem cell therapy, polyacrylamide hydrogels may serve as a protective and supportive matrix for stem cells, which are often susceptible to degradation and migration out of the target area when injected alone (as a matter of fact a majority of stem cells die within days after an intraarticular injection if injected without a membrane or a scaffold) [28]. This scaffold approach could aid in directing cell behavior, providing biochemical and mechanical cues that foster differentiation toward chondrogenic pathways and enhance cell viability [29,30].

Moreover, using hydrogels as a scaffold in combination treatments aligns with recent trends in tissue engineering, which emphasize the importance of a supportive matrix to encourage the regenerative potential of biological therapies. Such scaffolds not only create a microenvironment that supports cell growth but also offer controlled degradation and release profiles tailored to deliver cells and growth factors over extended durations [31]. The result could be a more effective, sustained healing response in the joint, reducing symptoms and delaying the progression of osteoarthritis [32].

To our knowledge, until this date no prior studies have been published on the combination of intraarticular injections of exosomes and polyacrylamide hydrogels in combination, our initial ultrasound examinations indicate a much faster regeneration compared to treatments with only stem cells or PRF, the patients also reported an improvement in pain symptoms faster than they would without the combination. The limitations of this small study prevented us from going into detail on this matter, larger more thorough studies on this combination with more measurable data would be helpful to further investigate this initial indication.

Despite the promising applications, further research is needed to determine optimal formulations, dosing,

Torbjörn Ogéus DC, et al., J Ortho Sports Med 2025
DOI:10.26502/josm.511500176

and delivery techniques for hydrogel-based combination therapies. Long-term studies on efficacy, safety, and potential adverse effects are essential before such treatments can become widely adopted in clinical practice. As this field evolves, polyacrylamide hydrogels may serve as a foundational component in the next generation of biologic-based joint therapies.

In our clinic more than 20 treatments with a combination of hydrogel, autologous stem cells and exosome injections have been performed in the last 4 months prior to the publication with promising results. The proposed scaffold-effect of the hydrogel is currently being evaluated and tested, a retrospective study on a larger patient group is being conducted presently with the hope that a larger portion of the injected stem cells survive after intraarticular injection.

Conclusion

In conclusion, based on the experience of this case series and a review of the current specialist literature, we advise that polyacrylamide hydrogel may be an effective intervention in the treatment of knee osteoarthritis. Especially in combination with other regenerative medicine interventions. Further research is required to test this theory.

Declaration

Ethics Approval

According to the Ethics Commission of Stockholm, Sweden, case reports with biological medicinal products do not require ethical approval for publication. This applies to the present study.

The study was conducted in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent for Publication

Written informed consent was obtained from the patients for the publication of these case reports and any accompanying data. Copies of the written consent forms are available for review by the Editor-in-Chief of this journal.

Funding

The author received no financial support for the research, authorship, and/or publication of this article.

Acknowledgements

The author was the main and only contributor to the manuscript.

Competing Interests

The author declares that he has no competing interests. However, he has held courses in injection techniques and ultrasound use in collaboration with Contura international A/S, the company that sells Arthrosamid™ the polyacrylamide hydrogel used in this case series.

Authors' contributions

TO was the patients primary caregiver regarding the specific injuries. All texts, design, literature review and drafting of these case reports was done by TO, responsible for the submitted manuscript.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files] are stored at the clinic and is available for review by the Editor-in-Chief of this journal.

References

1. Vos T, Abajobir AA, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet 390 (2017): 1211-1259.
2. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis and Cartilage 16 (2008): 137-162.
3. Caló E, Khutoryanskiy VV. Biomedical applications of hydrogels: A review of patents and commercial products. European Polymer Journal 65 (2015): 252-267.
4. Kolsgaard J, Nyvang J, Mechlenburg I, et al. A prospective cohort study of polyacrylamide hydrogel (Arthrosamid®) injection in patients with knee osteoarthritis. Osteoarthritis and Cartilage Open 3 (2021): 100160.
5. Uth K, Trifonov D. Polyacrylamide hydrogel reduces pain and improves physical function in knee osteoarthritis: a review of the literature and initial clinical experience. Journal of Pain Research 12 (2019): 1013-1018.
6. Lohmann P, Willuweit A, Nebelung S, et al. Polyacrylamide hydrogel shows a low inflammatory response and allows remodeling in a rabbit model of soft tissue augmentation. Journal of Materials Science: Materials in Medicine 28 (2017): 108.
7. Henrotin Y, Berenbaum F, Chevalier X. Clinical trial results of cross-linked hyaluronic acid injections in knee osteoarthritis: a review. International Journal of Clinical Rheumatology 12 (2017): 118-123.
8. Knee T, Mechlenburg J. Emerging injectable biomaterials for knee osteoarthritis. Biomaterials Science 8 (2020): 1025-1037.

Torbjörn Ogéus DC, et al., J Ortho Sports Med 2025
DOI:10.26502/josm.511500176

9. Ogéus T. Stromal Vascular Fraction with Platelet-Rich Fibrin for Osteoarthritis Management in Knee and Hip Osteoarthritis: A Retrospective 2-Year Follow-Up Study. Journal of Orthopedics and Sports Medicine 6 (2024): 135-143.

10. Ogéus T. Amniotic derived exosomes in the treatment of degenerative bone- and cartilage disease: A case series. Open J Orthop Rheumatol 9 (2024): 001-006

11. Fujioka-Kobayashi M. Schaller B, Mourão CFAB, et al. Biological characterization of an injectable platelet-rich fibrin mixture consisting of autologous albumin gel and liquid platelet-rich fibrin (Alb-PRF). Platelets 32 (2021): 74-81.

12. Bagno L, Hatzistergos KE, Balkan W, et al. Mesenchymal stem cell-based therapy for cardiovascular disease: progress and challenges. Mol Ther 26 (2018): 1610-23.

13. Lou G, Chen Z, Zheng M, et al. Mesenchymal stem cell-derived exosomes as a new therapeutic strategy for liver diseases. Exp Mol Med 49 (2017): e346-e.

14. Hassanzadeh A, Rahman HS, Markov A, et al. Mesenchymal stem/stromal cell-derived exosomes in regenerative medicine and cancer; Overview of development, challenges, and opportunities. Stem Cell Res Therapy 12 (2021): 297.

15. Miron RJ, Pinto NR, Quirynen M, et al. Standardization of relative centrifugal forces in studies related to platelet-rich fibrin. Journal of Periodontology 90 (2019): 817-20.

16. Fujioka-Kobayashi M, Katagiri H, Kono M, et al. Improved growth factor delivery and cellular activity using concentrated platelet-rich fibrin (C-PRF) when compared with traditional injectable (i-PRF) protocols. Clin Oral Investig 24 (2020): 4373-4383

17. Miron RJ, Pikos MA, Estrin NE, et al. Extended platelet-rich fibrin. Periodontol 94 (2023): 114-130.

18. Burger M, Degnan D. Comparative Safety, Efficiency, and Nursing Preference Among 3 Methods for Intravenous Push Medication Preparation: A Randomized Crossover Simulation Study. J Patient Saf 15 (2019): 238-245.

19. Ackerman I. Western Ontario and McMaster universities osteoarthritis index (WOMAC) Aust J Physiother 55 (2009): 213

20. McConnell S, Kolopack P, Davis AM. The western Ontario and McMaster universities osteoarthritis index (WOMAC): a review of its utility and measurement properties. Arthritis Rheum 45 (2001): 453-461.

21. Chim SM, Tickner J, Chow ST, et al. Application of polyacrylamide hydrogel in tissue engineering and regenerative medicine. Journal of Biomedical Materials Research Part B: Applied Biomaterials 101 (2013): 1561-1571.

22. Zhu J, Marchant RE. Design properties of hydrogel tissue-engineering scaffolds. Expert Review of Medical Devices 8 (2011): 607-626.

23. Hoffman AS. Hydrogels for biomedical applications. Advanced Drug Delivery Reviews 54 (2002): 3-12.

24. Shea LD, Wang D, Franceschi RT, et al. Engineered bone development from a pre-osteoblast cell line on three-dimensional scaffolds. Tissue Engineering 6 (2000): 605-617.

25. Huang J, Hu J, Chen F, et al. An updated review on the usage of PRP and stem cells in orthopaedic surgeries: Allogeneic vs autologous. American Journal of Translational Research 9 (2017): 2616-2626.

26. Filardo G, Kon E, Di Matteo B, et al. Platelet-rich plasma for the treatment of knee osteoarthritis: An interventional study. Arthroscopy: The Journal of Arthroscopic & Related Surgery 29 (2013): 792-800.

27. Sato M, Uchida K, Nakajima H, et al. Isolation and characterization of stem cells derived from the degenerated human intervertebral disc tissues. Stem Cells and Development 21 (2012): 893-902.

28. Maus U, Andereya S, Gravius S, et al. Cryopreserved amniotic membrane as a scaffold for cartilage tissue engineering: In vitro and in vivo studies. Biomedical Materials 3 (2008): 025001.

29. Frith JE, Mills RJ, Cooper-White JJ. Lateral spacing of adhesion peptides influences human mesenchymal stem cell behavior. Journal of Cell Science 125 (2012): 317-327.

30. Varghese S, Hwang NS, Ferran A, et al. Engineering musculoskeletal tissues with human embryonic stem cells. Biomaterials 31 (2010): 34-42.

31. Shin H, Jo S, Mikos AG. Biomimetic materials for tissue engineering. Biomaterials 24 (2003): 4353-4364.

32. Chen FM, Liu X. Advances in biomaterials for regenerative medicine. Materials Science and Engineering: R: Reports 100 (2016): 1-66.