

Modern Joint Preservation Using Biologics to Target Bone Edema





The Challenge

Individuals suffering from osteoarthritis coupled with bone marrow lesions have a ninefold higher likelihood of progressing to total knee arthroplasty within a three-year timeframe (1, 2, 3).

Many patients are seeking an alternative to more invasive joint replacement options.

Better Alternatives Are Needed to Salvage Joints

Presently, existing joint preservation methods frequently fall short, leading to a rapid increase in total knee arthroplasties (TKAs), especially among the aging population. For instance, multiple research studies have revealed that arthroscopic debridement, by itself, offers minimal advantage (4, 5). Similarly, treatments such as calcium phosphate and core decompression have not demonstrated any significant improvement over conservative therapy alone (6, 7, 8, 9). The ineffectiveness of calcium phosphate, in particular, has been attributed to its failure to stimulate new bone growth needed to repair the lesions (10).

Analysis of bone marrow aspirate samples extracted from areas of edema in damaged bone revealed the complete absence of osteo-progenitor cells (18). This scarcity of cellular elements partly elucidates the persistence of this chronic condition and underscores the potential efficacy of transplanting marrow enriched with osteo-progenitor cells.

The convergence of orthopedic science, immunology, and practical wisdom directs us back to the most reliable solution: utilizing cells sourced from the iliac crest marrow for the repair of damaged bone. In essence, the fundamental principle is clear - cells are the key to bone growth!





What Can the Literature Teach Us:

In a notable randomized controlled study focusing on patients scheduled for bilateral total knee arthroplasty (TKA), Hernigou et al. demonstrated the superior efficacy of biologic repair of bone edema. This was achieved using iliac crest-sourced marrow aspirate rich in osteo-progenitor cells, in comparison to TKA, over a significant follow-up period of 15 years. A crucial factor in the success of this treatment was the dose of osteo-progenitor cells administered, with doses exceeding 4,000 cells per mL identified as the average effective dose (11,12).

Out of 140 patients, only 18% of those who underwent the biologic repair on one side eventually required a TKA. The average time before undergoing TKA for these 18% was 10 years post-biologic repair. Furthermore, one year after the procedure, the biologically repaired knees showed better average scores on the Visual Analog Scale (VAS) for pain compared to those that underwent TKA. These patient-reported improvements were mirrored in disease modifications, as evidenced by MRI findings. Notably, the presence of persistent bone marrow lesions (BMLs) after biologic repair was identified as a significant independent risk factor for the need for subsequent TKA, with larger BMLs posing higher risks (11, 12).

The study's findings were further corroborated when repeated using the Cervos Marrow Cellution device. In this iteration, the knees that received biologic repair demonstrated statistically significant improvements across all follow-up periods in several key areas: the International Knee Documentation Committee scores, the Knee Injury and Osteoarthritis Outcome Score (subdivided into pain, activities of daily living, and quality of life), and the Visual Analog Scale for pain. Notably, no complications were reported in this follow-up study (13).

Cervos Case Report



Pre-op



6 Months Post-op



Can You Inject Both Intraarticular and Intraosseous?

In another study, Hernigou conducted a comparison between intraarticular or intraosseous injections in treating patients with painful bilateral knee osteoarthritis of similar severity. Over a 15-year follow-up period, only 20% of patients treated with intraosseous injections progressed to total knee arthroplasty (TKA), in stark contrast to 70% of those who received intraarticular treatments. Although both methods showed benefits, intraosseous treatment emerged as markedly more effective (22).



The approaches of intraarticular and intraosseous treatment are not necessarily exclusive. Considering the joint as an entire organ, which includes damage to both the trabecular bone and cartilage, it makes logical sense to address the entire scope of the pathology.

Clinicians have also reported, based on anecdotal evidence, improved results when treating the interface opposite chondromalacia on the trabecular bone side, in addition to the intraarticular side. The belief is that healthy bone plays a crucial role in nourishing the joint. Supporting this, MRI findings using the Cervos solution indicate that such a comprehensive treatment approach may yield more favorable outcomes.



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How can I Implement this Technique in my Practice?

A Common-Sense Approach:

- Repair intraosseous bone marrow lesions with the gold standard: Iliac crest sourced marrow
- Treat intraarticular chondromalacia with high-dose PRP

Obtaining the Biologic: Dose Matters

The procedure of Bone Marrow aspiration utilizing the Cervos Marrow Cellution system is known for being well-tolerated and is commonly conducted in an office setting using just local anesthesia. The process of aspirating a volume of 5 mL typically takes around two minutes and can be repeated if necessary for obtaining larger volumes. Notably, this technique does not require the use of a centrifuge. It consistently yields an aspirate that contains an osteo-progenitor cell count ranging from 4500 to 5500 per mL (13,14,15,16,17). It has been observed that higher concentrations of osteo-progenitor cells per mL, especially those exceeding 2,500, are linked to more favorable outcomes.

Platelet-Rich Plasma (PRP) therapy is a procedure that is widely accepted and often carried out in an office environment. Research indicates that high-dose PRP treatment, which involves delivering over 10 billion platelets, is effective in the management of knee osteoarthritis (OA) (19). Conversely, low-dose PRP has been found to be ineffective in treating knee OA (20). The Cervos PRP system, which begins with an 80cc draw of blood, consistently achieves the delivery of over 10 billion platelets, as evidenced by studies (21).







Delivering the Biologic

Targeting of damaged bone using a C-arm is common for larger bones, while ultrasound is preferred for smaller bones. This technique is well-established in the field.

The process of inserting a delivery cannula, typically done with an orthopedic drill, is a procedure that can be carried out in an office setting using only local anesthesia. This method is employed for the precise delivery of biologics.

The Cervos drill, designed for these procedures, is notable for its autoclavable feature and comes equipped with a rechargeable battery, enhancing its usability and convenience.

Additionally, Cervos Intraosseous Access cannulas are available in a variety of lengths and gauges. This range allows for flexible and easy access to different sites of bone edema, catering to diverse treatment needs.

Learn from the Experts:

Explore the potential of Cervos technology in revolutionizing joint preservation by inquiring about specialized educational workshops. These sessions are designed to equip you with the knowledge and skills needed to effectively integrate this advanced strategy into your practice. Don't miss this opportunity to be at the forefront of joint preservation – reach out to us and discover how Cervos technology can enhance your treatment capabilities.



About Cervos Medical

Cervos Medical, a subsidiary of Ranfac Corp, is a medical device company dedicated to pioneering innovative solutions in autologous biologics. Our state-of-the-art systems are designed to deliver biologics that emulate and enhance vasculogenesis, the body's innate repair mechanism. We specialize in developing minimally invasive, highly efficient, and cost-effective solutions. Our focus is on treating a wide range of conditions through bone repair, joint preservation, accelerated rejuvenation, and effective management of chronic pain, thereby advancing patient care and outcomes.









References

I. Pareek, Ayoosh MDI et al Spontaneous Osteonecrosis/Subchondral Insufficiency Fractures of the Knee, The Journal of Bone and Joint Surgery: May 6, 2020 - Volume 102 - Issue 9 - p 821-829

2. Dong B et al. Experimental and Therapeutic Medicine Severity and distribution of cartilage damage and bone marrow edema in the patellofemoral and tibiofemoral joints in knee osteoarthritis determined by MRI. Exp Ther Med. March 7, 2017.

3. Scher C, Craig J, Nelson F. Bone marrow edema in the knee in osteoarthrosis and association with total knee arthroplasty within a three-year follow-up. Skeletal Radiol 2008; 37 (7) 609-617

4. Moseley JB, O'Malley K, Petersen NJ , et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med 2002; 347 (2) 81-88

5. Kirkley A, Birmingham TB, Litchfield RB, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med 2008; 359 (11) 1097-1107

6. DeBernardis D et al Percutaneous Skeletal Fixation of Painful Subchondral Bone Marrow Edema of the Knee Arthroscopy, Sports Medicine and Rehabilitation Volume 2, Issue5, October 2020.

7. S.B. Cohen et al. Subchondroplasty for treating bone marrow lesions. J Knee Surg. 29 2016

8. Pareek, Ayoosh MD1 et al Spontaneous Osteonecrosis/Subchondral Insufficiency Fractures of the Knee, The Journal of Bone and Joint Surgery: May 6, 2020 - Volume 102 - Issue 9 - p 821-829

9. Nairn L et al Safety and early results of Subchondroplasty for the treatment of bone marrow lesions in osteoarthritis: a systematic review Knee Surgery, Sports Traumatology, Arthroscopy vol 29. 3599-3607.

10. Petronne B et al Subchondroplasty Bone Substitute Material (BSM) Histological Analysis after Total Knee Arthroplasty: A Case Series Journal of clinical case studies, reviews, & reports Research Article ISSN 2634-680X

11. Hernigou P, Delambre J, Quiennec S, Poignard A. Human bone marrow mesenchymal stem cell injection in subchondral lesions of knee osteoarthritis: a prospective randomized study versus contralateral arthroplasty at a mean fifteen year follow-up. Int Orthop. 2020 Apr 23. Epub ahead of print. PMID: 32322943

12. Hernigou P, Auregan J, Dubory A, Flouzat-Lachaniette C, Chevallier N, Rouard H. Subchondral stem cell therapy versus contralateral total knee arthroplasty for osteoarthritis following secondary osteonecrosis of the knee International Orthopaedics; 19 March 2018 13. Dallo I, Gobbi A, et al. Minimally invasive cell based therapy for symptomatic bone marrow lesions of the knee: a prospective clinical study at 1 year, Stem cells & development, DOI: 10.1089/scd.2021.0283

14. Scarpone M, Kuebler D, Chambers A et al (2019) Isolation of clinically relevant concentrations of bone marrow mesenchymal stem cells without centrifugation. Journal of Translational Medicine https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-018-1750-x

15. Scarpone M, et al Marrow Cellution: The Impact of Volume on Related Cell Counts Using The Marrow Cellution Bone Marrow Aspiration System. White Paper

16. Tortland P, et al Technique Matters: Small Draw, Diverse Geography, Precise Repositioning, Lateral Draws Only, Pace and Syringe Plunger Yields Clinically Relevant CFU-f Counts. White Paper

17. Lutz et al. Presented at The Orthobiologic Institute annual meeting in 2020.

18. Testing performed by Cervos and on file with the Company.

19. Bansal, H., Leon, J., Pont, J.L. et al. Author Correction: Plateletrich plasma (PRP) in osteoarthritis (OA) knee: Correct dose critical for long term clinical efficacy. Sci Rep 11, 18612 (2021).

20. Bennell KL, et al. Effect of Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients With Knee Osteoarthritis: The RESTORE Randomized Clinical Trial. JAMA. 2021 Nov 23;326(20):2021-2030

21. Critial Role of High Dose PRP in Clinical Practice. Cervos White Paper

22. Hernigou P, Bouthors C, Bastard C, Flouzat Lachaniette CH, Rouard H, Dubory A. Subchondral bone or intra-articular injection of bone marrow concentrate mesenchymal stem cells in bilateral knee osteoarthritis: what better postpone knee arthroplasty at fifteen years? A randomized study. Int Orthop. 2020 Jul 2.