CERVOS MEDICAL

White Paper

Understanding the Critical Role of High-Dose PRP in Clinical Practice

The Challenge

Platelet Rich Plasma (PRP) is widely used across different specialties but the opinion within academia is mixed as to PRP's clinical effectiveness. Several studies have demonstrated that PRP does not provide a benefit compared to a control arm of saline or conservative therapy alone.[2,9,11] Other studies demonstrate the opposite, with the PRP arm being statistically superior to the control. With such conflicting evidence, choosing the right PRP system can be a significant challenge for providers looking to achieve the best outcomes.

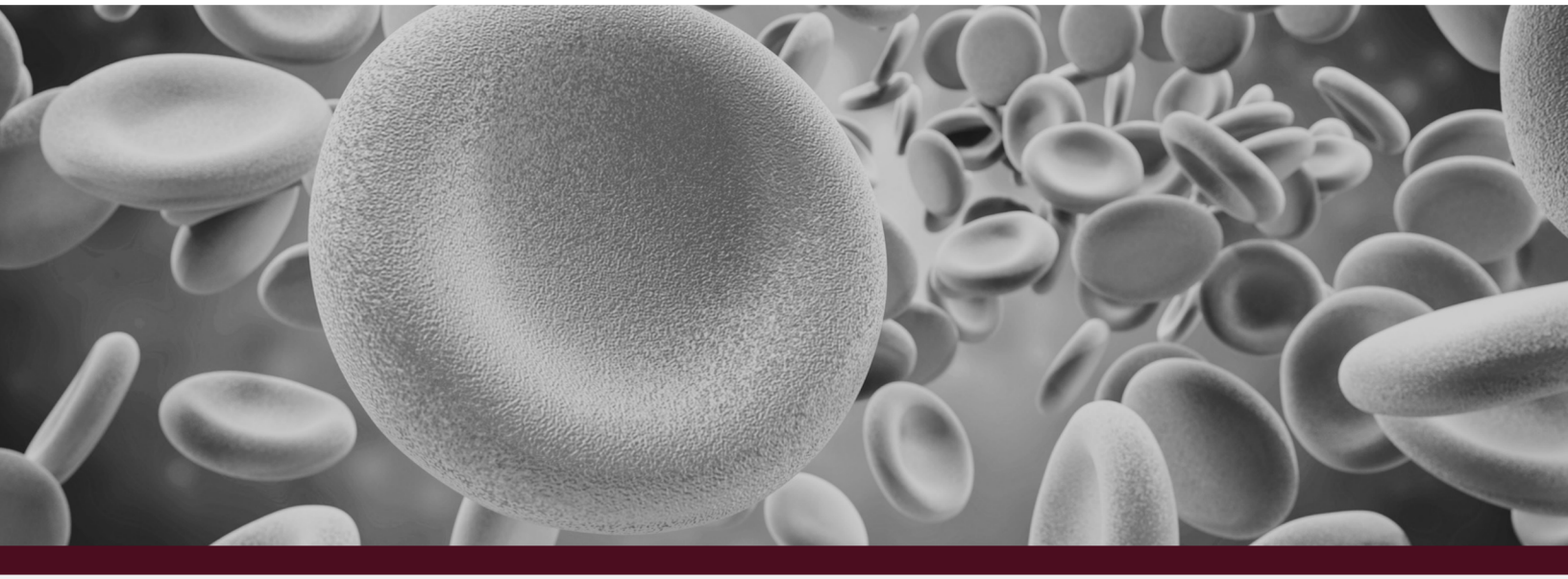
How Did We Get Here

PRP was introduced to the regenerative medicine community in the early 2000s and was dominated by commercial devices based on modified blood banking equipment and protocols, many of which were not originally intended to make PRP. The phrase "PRP" became a catch-all for a variety of different biologic therapies that varied greatly from device to device.

Therefore, comparing one PRP study to another is not meaningful because the treatments varied significantly, with the only common feature being the catch-all phrase "PRP". As a result, the number of preparation protocols continues to grow, including inadequate PRP treatments that fail to produce meaningful results.[9, 10, 11]

The Unenviable Position of the Clinician

Many patients are aware of and inquire about PRP and regenerative medicine procedures. These therapies are often advertised and are the topic of discussion in numerous news outlets. However, with a market dominated by numerous different PRP options and a body of literature that is mixed on the efficacy of PRP, how do you make the right choice for your practice and your patients?



A Common Sense Approach

Cell therapy was first used in hematology and oncology for bone marrow rescue therapy in the background of irradiation or immune conditioning. After determining an HLA match, the most important characteristic of the biologic was the dose of hematopoietic stem cells (HSCs) in the graft. A dose below the critical threshold leads to tragic outcomes.

In orthopedics, the theme of dose was again shown to be insightful, as any graft that had a dose of osteoprogenitor cells below a certain threshold resulted in a failed bony union or soft-tissue-to-bone repair. It would seem logical that since the human body responds to doses in other areas of medicine, PRP should be no different.

What Can the Literature Teach Us?

A consistent theme in the literature across different musculoskeletal (MSK) ailments is that high-dose PRP is effective and low-dose PRP does not work. A recent study found that PRP products must contain at least 10 billion platelets to provide improved relief for osteoarthritis of the knee versus HA. Most preparations produce less than half this amount.[1]

Additionally, low-dose PRP has not been shown to achieve better results than saline or hyaluronic acid.[2,10] These are just a few of the growing number of studies demonstrating that a high-dose of PRP is key to achieving the best healing results.

What is High-dose PRP?

PRP is often measured by the number of platelets delivered (usually in the billions) or the increase over baseline, which is calculated by dividing the number of platelets per mL in the PRP by the number of platelets in native blood. A rule of thumb is you want a minimum of 1 billion platelets per mL and on average at least 1.5 billion platelets per mL.[5] Another general guideline is to aim for a 7x to 10x increase over baseline for patients 55 and younger, but 15x or higher for patients over 55.[6] With a more concentrated PRP product, damaged tissues receive a greater number of biomolecules, including platelets and growth factors, that stimulate natural healing cascades.[6] In short, a higher dose means better outcomes.[1,8]

"Across a sample of 70 consecutive patients treated and starting with a 60 mL blood draw and volume reducing that to 5 mL of PRP using the Cervos system, the average platelet count was 1689 million/mL representing a 7.15x increase over baseline."
–Paul Tortland, MD

Can High-dose PRP Cause Harmful Side Effects?

We are not aware of a single study in orthopedics where treating avascular tissues with higher doses has led to a harmful side effect. If such a dose exists, we have not reached that threshold. The more likely negative outcomes would be those associated with low-dose PRP, as these patients do not receive the highest quality of treatment.

A Call to Action

Patients should only be treated with high-dose PRP. It would be negligent to irradiate a patient and then treat them with a low-dose marrow transplant, basically ensuring their demise. While PRP is not resulting in untimely deaths, medical literature has shown that low-dose PRP can result in less-than-optimal outcomes for patients.

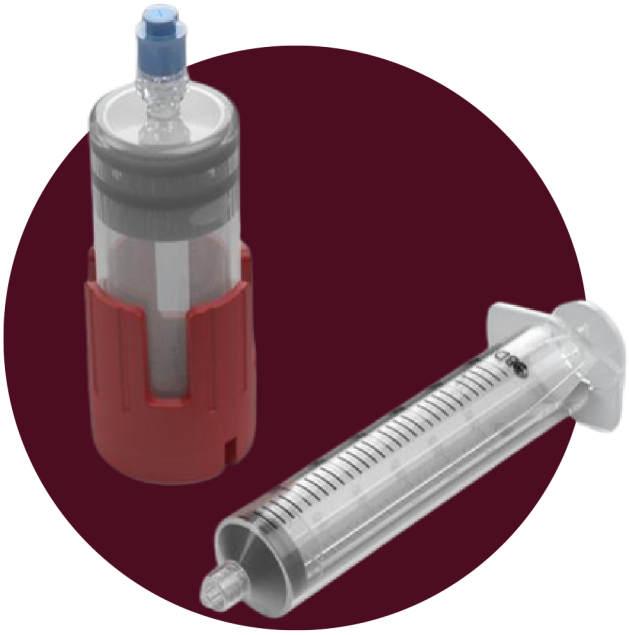
Economics Matter in Healthcare Today

If you had a hole in the roof of your house, you would fix it regardless of whether insurance paid for it or not. Many patients take this common sense approach and pay for PRP out of their own pockets, as insurance often does not cover the procedure. This reality puts pressure on providers to not only give the best care but also do it affordably.

Choosing a cost-effective PRP system helps patients save money on treatment while reducing operating costs for providers. The challenge is finding such a system that also produces a high-quality, high-dose PRP product.

The Solution: Cervos KEYPRP

The Cervos KEYPRP System produces high-dose PRP by maximizing platelet collection following proven blood banking protocols such as a double spin for optimal platelet recovery. High-dose PRP is particularly suitable for older patients.[6,7] The system is cost-effective, user-friendly, and minimizes risk of contamination. With benefits for both patients and providers, the Cervos KEYPRP system is leading the way in PRP and regenerative medicine innovation.



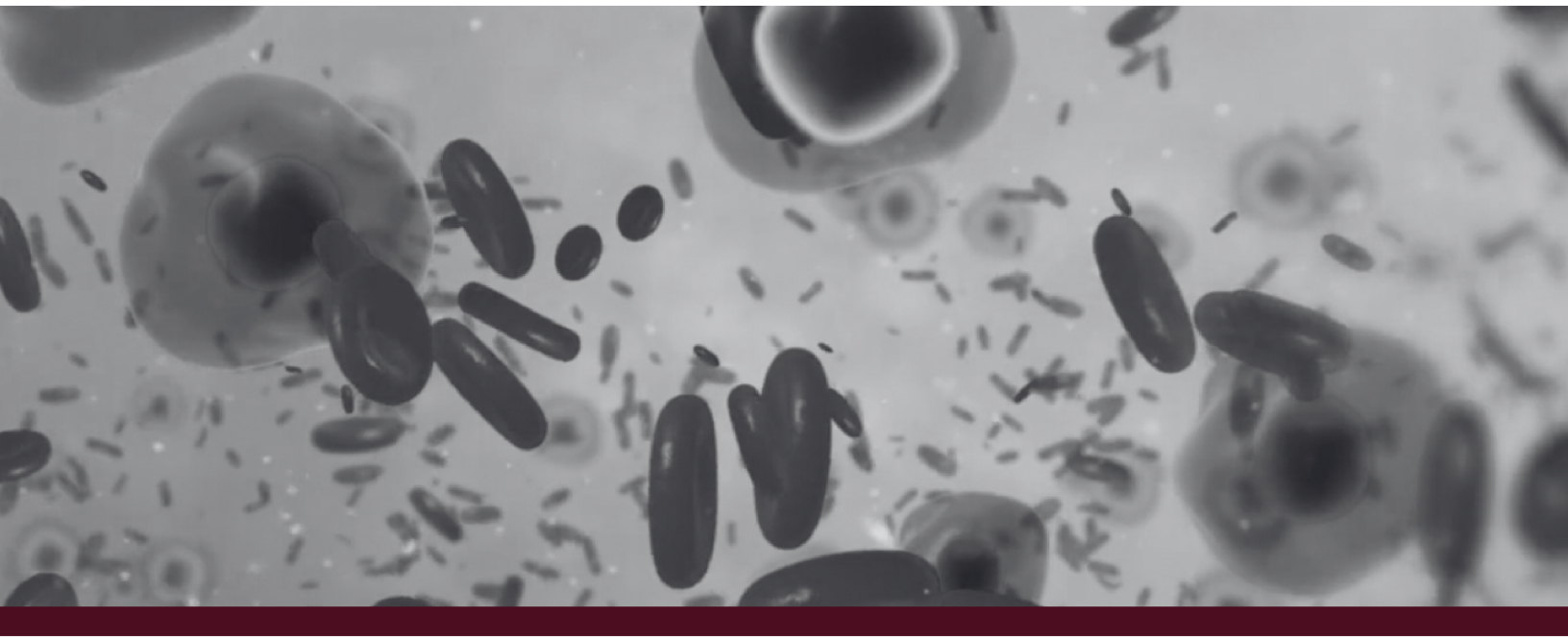
Maximum Platelet Recovery

KEYPRP's proprietary concave platelet collection surface delivers industry-leading platelet recovery and the highest increase over baseline — while controlling hematocrit. This increase over baseline can reach up to 50 times. The unique platelet collection surface allows providers to determine the best cell composition for each patient. Each PRP product can have different amounts of platelets, hematocrit, white blood cells, lymphocytes, monocytes, and neutrophils.[3]

KEYPRP also optimizes growth factor concentration that attracts regenerative cells to the treatment site. A high-dose of growth factors and platelets work to boost the local immune response to protect vulnerable tissues.[6]

Customizable Protocols

To accommodate each patient's individual needs and treatment goals, the KEYPRP system allows providers to customize input and output volumes, hematocrit, neutrophil content, and increases over baseline. The system offers both single-spin and double-spin protocols that are used to control for varying levels of each target cell type in the PRP.[3,4,5]



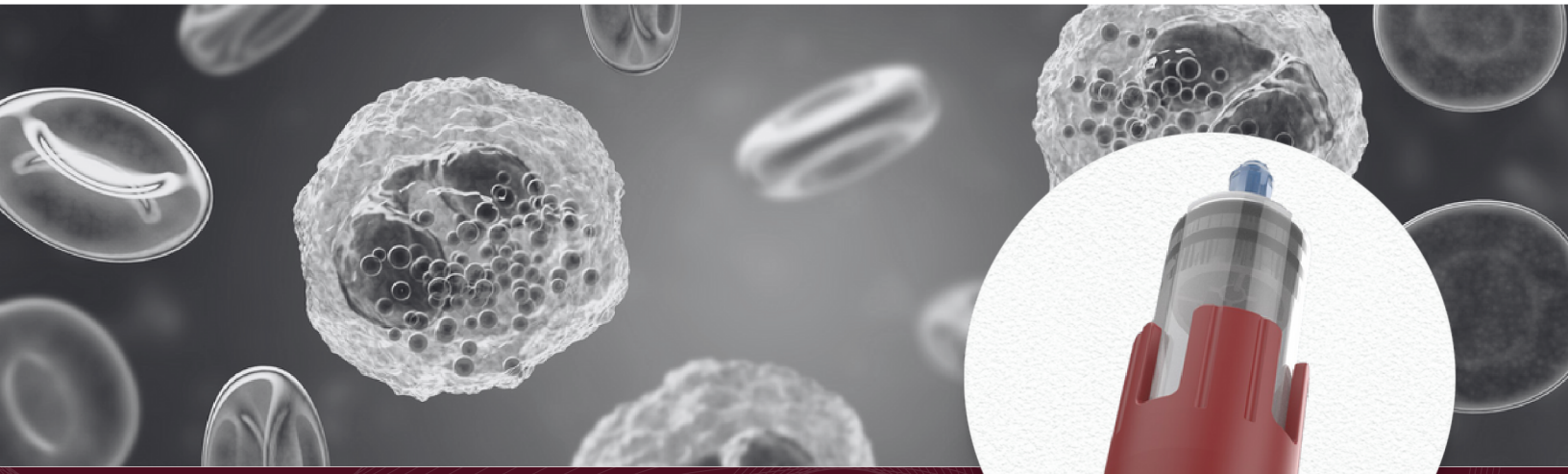
Leukocyte Poor Preparations

Many clinicians use LP-PRP in a joint space with the goal of maximizing the recovery of platelets and lymphocytes and minimizing neutrophils and hematocrit. The Key PRP system uses a two spin protocol with a manual decant that allows the user to precisely control for these variables that produces a PRP with a hematocrit of less than 1/10 of one percent while also hitting target platelet recoveries of over 1.5 billion platelets per ml.[5]

Leukocyte Rich Preparations

KEYPRP produces a leukocyte-rich concentration high in platelets, lymphocytes, monocytes, and neutrophils. Neutrophils are the most pro-angiogenic cell within blood that release large amounts of VEGF and are anti-inflammatory in the presence of elevated platelets. Many clinicians use this type of PRP outside of a joint at places of tendon to bone injury.[12,13,14,15,16]

Numerous recent publications have demonstrated the importance of these cells in various clinical settings. The KEYPRP system leverages the flexibility of a controlled decant to create a unique PRP preparation, with up to 50X native levels of platelets.[12,13,14,15,16]



About Cervos Medical

Cervos Medical is a procedure-driven medical device company focused on innovative solutions to improve natural healing. Our best-in-class autologous and synthetic orthobiologic products mimic and promote vasculogenesis, the body's natural reparative mechanism. We develop minimally invasive, highly efficient, and cost-effective solutions that treat a variety of musculoskeletal conditions by repairing bone, preserving joints, and managing chronic pain.

info@cervos.com
https://www.cervos.com/
(844) 830-4050

References

1. Bansal, H., Leon, J., Pont, J.L., Wilson, D.A., Bansal, a., Agarwal, D., Preoteasa, I. (2021). Platelet-rich plasma (PRP) in osteoarthritis (OA) knee: Correct dose critical for long term clinical efficacy. Scientific Reports 11, 18612.
2. Wang, Y.C., Lee, C.L., Chen, Y.J., Tien, Y.C., Lin, S.Y., Chen, C.H., Chou, P.P.H., Huang, H.T. (2022). Comparing the Efficacy of Intra-Articular Single Platelet-Rich Plasma (PRP) versus Novel Crosslinked Hyaluronic Acid for Early-Stage Knee Osteoarthritis: A Prospective, Double-Blind, Randomized Controlled Trial. Medicine 58, 1028.
3. Platelet Rich Plasma (PRP) / Platelet Concentrate (PC) Systems: Preparation Processing Protocols. Christopher Kyriakides, DO. Department of Rehabilitation Medicine. NYU Grossman School of Medicine.
4. Optimizing PRP / PC Preparation: Treatment of Degenerative Disc Disease (DDD) – Dose Matters. Gregory E Lutz. MD. Regenerative Sports Care Institute. NYC.
5. Dose Matters. Paul D Tortland, DO, FAOASM RMSK. Associate clinical professor of medicine. University of Connecticut School of Medicine
6. Platelet lysates from aged donors promote human tenocyte proliferation and migration in a concentration – dependent manner. Berger et al. Bone and Joint res. 2019. Feb. 2. 8(1) 32-40.
7. Clinical outcome and risk factor predictive for failure of autologous PRP injections for low-to-moderate knee osteoarthritis. Massola et al journal of Orthopedic Surgery. 29(2) 1-7.
8. Platelet-Rich Plasma Injections for the Treatment of Hamstring Injuries. Hamid M et al. Am J Sports Med. 2015 May; 43(5)
9. Platelet-rich plasma does not enhance return to play in hamstring injuries: a randomized controlled trial. Hamilton B et al BR J Sports Med 2015 Jul;49(14):943-50.
10. 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. Bennell K et al. November 23: 2021: Jama 326(20) 2021-2020.
11. Platelet-Rich Plasma for Patellar Tendinopathy: A Randomized Controlled Trial of Leucocyte-Rich PRP or Leukocyte-Poor PRP Versus Saline. Scott A et al AOSSM. Vol.47, issue 7.
12. Leukocyte -rich PRP versus leukocyte -poor PRP – The role of monocyte/macrophage function in the healing cascade. Lana J. et al. J Clin Ortho Trauma. 2019 Oct. 10 (Suppl 1) S7-S12
13. The role of the macrophage in tendinopathy and tendon healing. Sunwoo J et al. Journal of Orthopedic Research. 19, March 2020.
14. Engineering Neutrophil Immunomodulatory Hydrogels Promoted Angiogenesis. Gao Z et al. ACS Appl. Material Interfaces 2022 14,35 39746-397758.
15. Case Report: Clinical outcomes following injections of leukocyte-rich platelet-rich plasma in osteoarthritis patients Kenmochi M et al Journal of Orthopedics vol. 18 March-April 2020. Pg 143-149
16. Platelets and Granulocytes, in particular Neutrophils for important compartments for circulating vascular endothelial growth factor. Kusumanto et Angiogenesis 6(4):283-287 2004.