

CLINICAL WHITE PAPER

Beyond Standard PRP: Recovering the Therapeutic Fraction That Gets Thrown Away

How SuperShot PRP Concentrates Extracellular Vesicles, to Include Autologous Exosomes, and Signaling Proteins to Amplify and Sustain Orthobiologic Outcomes

Executive Summary

Platelet-rich plasma (PRP) is among the most widely used orthobiologic therapy in musculoskeletal medicine, offering a minimally invasive, autologous approach to tissue repair. However, the standard PRP preparation process is inherently incomplete. During centrifugation, the platelet-poor plasma (PPP) fraction, commonly discarded after PRP extraction, is now recognized as a rich reservoir of extracellular vesicles (EVs), including exosomes, microRNA (miRNA) cargo, signaling proteins, and growth factors too small to concentrate at conventional centrifuge speeds.

SuperShot PRP addresses this gap directly. By capturing and concentrating the autologous EV fraction that standard PRP leaves behind, SuperShot delivers a more complete biological preparation. The clinical case for this enhancement is supported by real-world outcome data from the DataBiologics registry, a multi-center dataset spanning 9 independent clinics, showing that patients treated with PRP plus an autologous EV fraction achieve meaningfully greater and more durable pain reduction than those treated with standard PRP alone.

At 24 months post-injection, patients in the SuperShot PRP cohort experienced a 57% reduction in Numeric Pain Rating Scale (NPRS) scores, compared to 38% for standard PRP, a 19-percentage-point advantage that continued to widen over time. This white paper reviews the scientific rationale, the mechanism of action, and the clinical outcome data supporting the use of SuperShot PRP in orthobiologic practice.

1. The Standard PRP Procedure and Its Biological Limitations

PRP therapy relies on centrifugation to separate whole blood into three primary fractions by density: red blood cells (RBCs) at the bottom, platelet-rich plasma (PRP) in the middle, and platelet-poor plasma (PPP) at the top. The PRP fraction is harvested and injected, delivering concentrated platelets (typically 4–5× baseline), growth factors such as PDGF, TGF- β , VEGF, and IGF-1, as well as cytokines and repair-signaling molecules that are released rapidly upon platelet activation.

The biological value of these platelet-derived mediators is well established. Meta-analyses and systematic reviews demonstrate that PRP injections produce significant pain reduction and functional improvement in knee osteoarthritis, tendinopathies, and related musculoskeletal conditions, often outperforming corticosteroids and hyaluronic acid, particularly for mild to moderate disease.¹²

However, a critical limitation of standard PRP is the **centrifuge speed required to pellet exosomes**. Exosomes and small EVs (30–150 nm) require ultracentrifugation forces of 100,000×g or greater to be concentrated.³ Standard PRP centrifuge protocols operate at far lower g-forces, typically 300–3,000×g -and therefore are physically incapable of capturing this sub-fraction. The result is that the PPP layer, typically discarded in standard workflow, retains the majority of the patient's autologous EV payload.

2. What Is Left Behind: The PPP Fraction

The platelet-poor plasma fraction has historically been regarded as a biological byproduct, waste plasma with minimal therapeutic value. This view is now being actively challenged by peer-reviewed research demonstrating that PPP is, in fact, a meaningful source of small EVs with potent anti-inflammatory and regenerative properties.

A 2024 study published in the Journal of Orthopaedic Surgery and Research specifically characterized extracellular vesicles derived from platelet-poor plasma (PPP-EVs) and examined their effects on human osteoarthritic chondrocytes stimulated with interleukin-1 β (IL-1 β), one of the primary drivers of joint inflammation and cartilage degradation. The investigators found that PPP-EVs:

- Significantly decreased the expression of inflammatory genes in stimulated chondrocytes
- Robustly upregulated COL2A (collagen type II) and ACAN (aggrecan), key chondroprotective markers
- Modulated the catabolic microenvironment of osteoarthritic joints

The authors concluded that PPP-derived extracellular vesicles represent *"an affordable and promising option to modulate the catabolic microenvironment of osteoarthritis chondrocytes."*⁴

The PPP fraction, typically discarded in a standard PRP procedure, contains a potent reservoir of autologous extracellular vesicles with documented anti-inflammatory and chondroprotective activity.

3. Exosomes and Extracellular Vesicles: Biology and Mechanism

3.1 What Are Exosomes?

Exosomes are a subclass of extracellular vesicles, typically 30–150 nm in diameter, generated when multivesicular endosomes fuse with the cell membrane and release their internal vesicles into the extracellular space.⁵ They are produced by virtually all cell types in the body, including platelets, endothelial cells, and mesenchymal cells. Exosomes serve as biological communication packets, carrying and transferring nucleic acids (particularly microRNA), proteins, lipids, and growth factors between cells.

3.2 MicroRNA: The Biological Instruction Packets

The most therapeutically significant cargo carried by exosomes is microRNA (miRNA), small, single-stranded non-coding RNA molecules (approximately 22 nucleotides) that regulate gene expression at the post-transcriptional level.⁶ Once delivered to a recipient cell via exosomal fusion, miRNA can suppress or activate specific genetic pathways governing:

- Inflammation (downregulating pro-inflammatory cytokines such as TNF- α , IL-1 β , IL-6)
- Angiogenesis (promoting new blood vessel formation to support tissue healing)
- Cell proliferation and differentiation (stimulating regenerative cell activity)
- Tissue remodeling (regulating extracellular matrix synthesis and degradation)

Platelet-derived exosomes are particularly enriched in specific miRNAs. Key candidates including miR-21, miR-223, miR-214, and miR-155 have been identified as regulators of cytokine secretion and inflammatory signaling within the musculoskeletal microenvironment.⁷ Compared to platelet growth factors, which are released in a burst following activation and act over a relatively short window, exosomal miRNA cargo has the potential to produce prolonged downstream effects by reprogramming the gene expression of recipient cells.

3.3 Exosomes vs. Standard PRP Growth Factors

Property	Standard PRP Growth Factors	Exosomal miRNA / EVs
Mechanism	Receptor binding, signaling cascade	Gene expression regulation via miRNA
Time to effect	Rapid (hours–days post-activation)	Sustained (days–weeks)
Durability	Short-lived; degrades after activation	Prolonged downstream effect
Key molecules	PDGF, TGF- β , VEGF, IGF-1	miR-21, miR-32, miR-96, miR-142 (+ dozens more)
Size	Soluble proteins (~kDa range)	30–150 nm vesicles
Captured by standard PRP?	Yes	No -requires >100,000 $\times$ g

4. The SuperShot PRP Difference

SuperShot PRP is designed to capture what standard PRP discards. After the conventional PRP spin, the PPP fraction, instead of being wasted, is subjected to an additional processing step that

exploits a fundamental difference in the physical chemistry of plasma components: two-phase aqueous separation.

4.1 The Physics of Two-Phase Aqueous Separation

Two-phase aqueous separation is a partitioning technique in which two immiscible aqueous solutions, typically a polymer-salt or polymer-polymer system, create distinct phases with different affinities for biomolecules based on their size, surface chemistry, and density. When the PPP fraction is introduced into this system and subjected to a controlled third spin, small extracellular vesicles and exosomes preferentially partition into one phase while larger plasma proteins and solutes remain in the other.

This is a physics-driven separation, not a filtration event. Rather than relying on pore size to physically block or pass particles, two-phase aqueous separation exploits thermodynamic partitioning, the tendency of nano-scale vesicles to migrate toward the interface or into the phase that minimizes their surface energy. This allows exosomes and small EVs in the 30–150 nm range to be concentrated from the PPP without requiring the 100,000×g ultracentrifugation that makes laboratory-scale exosome isolation impractical in a clinical setting.

The result is a triple-spin workflow: the first two spins produce standard PRP and PPP fractions; the third spin, using two-phase aqueous separation, concentrates the autologous EV payload from the PPP into a film or pellet. The final preparation combines the PRP fraction with this EV-enriched fraction, delivering the complete autologous biological signal that a standard two-spin protocol leaves behind.

SuperShot's two-phase aqueous separation is a physics-based partitioning mechanism, not filtration. It leverages thermodynamic phase affinity to selectively concentrate exosomes and small EVs without ultracentrifugation, making autologous exosome recovery practical at the point of care.

This approach requires no additional blood draw, no allogeneic or manufactured product, and no regulatory concerns. The patient receives only their own biology, more completely recovered. The same device and protocol were used consistently across all 9 clinics contributing to the DataBiologics registry analysis described below.

5. Clinical Evidence: DataBiologics Multi-Center Registry

5.1 Study Design

The clinical outcomes data presented here derive from the DataBiologics outcomes registry, a prospective, multi-center database that tracks real-world orthobiologic treatment results using standardized patient-reported outcomes. The analysis compared two treatment cohorts:

- Standard PRP alone
- SuperShot PRP: PRP combined with the autologous EV fraction to include exosomes captured via the same device across all participating sites

The SS PRP dataset was drawn from 9 independent clinics. Various PRP systems were used across sites; however, the same device was used universally to capture the EV fraction, providing

methodological consistency in the EV/exosomal component. Both cohorts demonstrated matched baseline pain scores and identical Total Deliverable Platelets (TDP) at 11.2B, establishing strong comparability between groups.

Parameter	Standard PRP	SuperShot PRP
Cases	16,903	317
Patients	12,866	238
Baseline NPRS	4.72	4.73
TDP	11.2B	11.2B
Contributing Sites	Registry-wide	9 Clinics

Pain was measured using the Numeric Pain Rating Scale (NPRS), a validated 0–10 patient-reported outcome measure. The minimum clinically important difference (MCID) for NPRS is defined as a ≥2-point reduction. Follow-up time points were collected at 1, 3, 6, 12, 18, and 24 months post-injection.

5.2 Overall Cohort Results: Divergence Widens Over Time

Both treatment cohorts showed clinically meaningful pain reduction across all time points. However, a progressive divergence emerged that widened significantly by 24 months:

Timepoint	Standard PRP (% Pain Reduction)	SS PRP (% Pain Reduction)	Advantage for SS PRP
12 months	–36% (n=3,912)	–47% (n=82)	+11 percentage points
24 months	–38% (n=1,973)	–57% (n=52)	+19 percentage points

Standard PRP patients achieved meaningful early relief but plateaued around 36–38% pain reduction by 12 months, with minimal continued improvement through 24 months. In contrast, SS PRP patients demonstrated continuous improvement over the full two-year period, ultimately achieving a 57% pain reduction, nearly double the improvement seen in the PRP-only group at two years.

PRP provides the initial signaling burst. The autologous EV fraction sustains and amplifies the regenerative response, with the performance gap continuing to widen through 24 months.

5.3 Results by Anatomic Region

The advantage of SS PRP was observed across multiple anatomic sites, with the hip cohort showing the most striking long-horizon separation:

Anatomy	PRP 24-mo Reduction	SS PRP 24-mo Reduction	Boost
Hip	-42% (n=350)	-67% (n=10)	+25 points
Knee	~-29% (n=748)	~-58% (n=15)	+29 points
Shoulder	-46% (n=298)	-59% (n=14)	+13 points

For the hip, the 24-month difference achieved statistical significance ($p=0.019$ by Welch's two-sample t-test), despite relatively small sample sizes in the SS PRP arm. The shoulder cohort showed a statistically significant advantage at 12 months ($p=0.010$). The magnitude of benefit was consistent across these anatomically diverse indications, suggesting a systemic rather than site-specific mechanism.

5.4 Results by Diagnosis Category at 24 Months

Diagnosis Category	PRP (% Pain Reduction)	SS PRP (% Pain Reduction)	SS PRP Boost
Bone & Joint Degeneration	30% (n=1,130)	59% (n=15)	+29 points
Tendon Conditions	50% (n=599)	67% (n=24)	+16 points
Cartilage & Ligament	38% (n=314)	46% (n=8)	+8 points

The largest benefit was observed in the bone and joint degeneration category, which includes osteoarthritis, the most prevalent musculoskeletal condition and the primary indication for PRP in clinical practice. At 24 months, SS PRP patients in this category experienced nearly double the pain reduction (59% vs. 30%) compared to standard PRP, consistent with published in vitro evidence demonstrating PPP-derived EV anti-inflammatory activity in osteoarthritic chondrocytes.

These findings are also consistent with the growing body of preclinical literature demonstrating that PRP-derived exosomes promote tenogenesis in tendon stem/progenitor cells,⁸ support rotator cuff healing,⁹ and enhance muscle regeneration by establishing a pro-regenerative microenvironment.¹⁰

5.5 MCID Analysis: More Patients Reaching Clinically Meaningful Relief

Beyond average pain scores, the registry analysis examined the proportion of patients achieving the minimum clinically important difference (MCID) -defined as a ≥ 2 -point NPRS reduction. This metric captures whether individual patients experience clinically meaningful benefit, as opposed to statistical averages that may obscure responder patterns.

In the knee cohort, the SS PRP arm showed a growing advantage in MCID attainment over time. While early time points (1–12 months) showed near-parity, by 18 and 24 months the SS PRP advantage grew substantially:

- 18 months: +11 percentage-point MCID advantage for SS PRP (67% vs. 56%)
- 24 months: +21 percentage-point MCID advantage for SS PRP (80% vs. 59%)

At 24 months, 80% of SS PRP knee patients had achieved the MCID threshold, compared to 59% for standard PRP. This represents a 1-in-3 increase in the probability of a patient achieving meaningful clinical improvement.

6. Proposed Mechanism: Why Does SuperShot PRP Outperform?

The temporal pattern of divergence in the registry data, equivalent early results followed by progressive separation in favor of SS PRP, is mechanistically consistent with what is known about the biology of each component:

Standard PRP growth factors (PDGF, TGF- β , VEGF, etc.) are released rapidly upon platelet activation. They bind to surface receptors, initiate cell signaling cascades, and drive acute tissue repair responses. This is a potent but time-limited signal, growth factor concentrations decay over hours to days, and the signaling effect diminishes accordingly.

Autologous exosomal miRNA operates through an entirely different mechanism and timescale. Once delivered intracellularly via exosomal membrane fusion, miRNA directly modulates gene expression, effectively reprogramming the target cell's behavior for an extended period. A microRNA array comparison of standard PRP versus SS PRP preparations confirmed that SS PRP produces substantially greater upregulation of multiple miRNA species, including miR-32-5p and miR-142-3p -both implicated in inflammation resolution and tissue homeostasis.

This two-phase mechanism, a rapid initial repair signal from PRP, followed by a sustained gene-regulatory effect from exosomal miRNA, explains why the performance gap in the registry data continues to widen over 24 months rather than stabilizing. Published research on exosomal biology in musculoskeletal applications supports this model: exosomes derived from platelet sources have been shown to influence inflammation, angiogenesis, and extracellular matrix remodeling through miRNA-mediated gene regulation,⁷ consistent with the prolonged symptom improvement trajectory observed in the SS PRP cohort.

7. Multi-Center Validation and Generalizability

A critical strength of the DataBiologics dataset is its multi-center design. The SS PRP outcome data were contributed by 9 independent clinical sites, with varied PRP systems in use across practices, yet the same EV capture device was used universally. This design controls for EV/exosome preparation variability while reflecting the real-world heterogeneity of clinical environments (patient populations, injecting physicians, imaging guidance protocols, rehabilitation regimens).

The consistency of the SS PRP advantage across geographically and operationally diverse sites substantially increases confidence that the observed benefit reflects the EV (to include exosomes) fraction itself, rather than any site-specific confound. The matched baseline NPRS scores (4.72 vs. 4.73) and identical TDP values between cohorts further support the comparability of the two groups.

While the SS PRP cohort is smaller than the standard PRP comparator by design (reflecting current adoption rates), the registry-wide sample size, the use of matched baseline metrics, and the magnitude of observed differences collectively provide a clinically meaningful signal, particularly given that the data is derived from real patients in actual practice conditions rather than a controlled trial setting.

8. Conclusion

Standard PRP is a proven orthobiologic therapy, but it is an incomplete one. The conventional preparation workflow systematically discards the platelet-poor plasma fraction, and with it, a substantial reservoir of extracellular vesicles to include autologous exosomes, and microRNA that have documented anti-inflammatory, chondroprotective, and tissue-remodeling activity.

SuperShot PRP recovers this lost fraction at the point of care, delivering a more complete autologous orthobiologic preparation. The clinical evidence from the DataBiologics multi-center registry demonstrates that patients treated with PRP plus an autologous EV/exosome fraction achieve greater pain reduction, more patients reaching the minimum clinically important difference, and a trajectory that continues to improve through two years, while standard PRP plateaus.

The mechanistic explanation is coherent: PRP growth factors produce the initial repair burst; exosomal miRNA sustains the regenerative signal through long-duration gene regulation. Together, they address what neither can accomplish alone.

By recovering what standard PRP throws away, SuperShot delivers a more complete biological preparation, one that the data suggest improves patient outcomes in a clinically and statistically meaningful way across multiple anatomic sites and diagnoses.

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This white paper is intended for healthcare professionals. Clinical data from the DataBiologics outcomes registry.

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